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From the Dean



WHEN I WAS A YOUTH, I PLAYED THE CLARINET. It's an expressive instrument, capable of producing sounds that many say resemble the tone and dynamics of the human voice. Just as a person's voice becomes a personal signature, the clarinet produces a sound that's distinctive, recognizable from those of others in the woodwind crowd.

The degree to which we are distinguished by our voices is central to the stories in this issue of *Harvard Medicine*. We've tuned in to the complexities of the voice and vocal structures—what it means to lose voice, regain voice, or change voice to reflect an inner self.

To explore this topic, we've brought you stories of what our community of physicians and scientists is doing to unravel how and why neurodegenerative diseases so often rob patients of voice as well as how innovations in the field of laryngology are helping to restore the voices of those who have suffered disease, damage, or trauma. To complement stories of voices lost, we've presented those of voices found, either in patient-centered clinical encounters or in the development of compassionate approaches to palliative care.

The importance of the transformed voice also has a place in this issue. Here, we've considered how voice and speech therapy can help individuals seeking to shape their voices to aid in gender affirmation. And we celebrate what the voice, in song, can bring to the life of a physician.

How vital voice and vocal expression are to presenting oneself gained special significance for me recently: I became a grandfather for the second time. I find myself talking with my grandson in a voice that generations of grandfathers have no doubt used: soft tones and gentle cadences that I hope will soothe. He, in turn, shares coos and burbles that tell me, or at least my daughter, what he needs, how he feels, and, perhaps, even what he thinks about the new world he finds himself in. He is bringing his voice to this world, and we listen, rapt.

A handwritten signature in dark ink, appearing to read 'Jeffrey S. Flier'.

Jeffrey S. Flier
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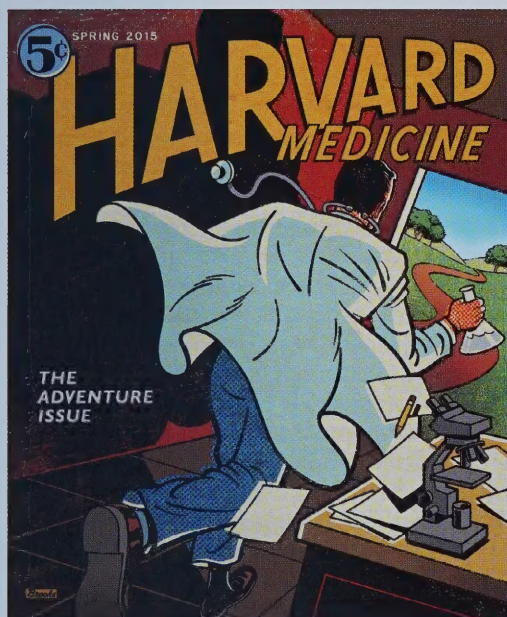
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Letters to the Editor

CHART NOTES FROM OUR READERS



Group dynamics can be unpredictable, but the Class of 1980 showed it has a mix of creative, talented, caring individuals who bring out the best in one another.

SHARON ANN CLARK '80
SAN MATEO, CALIFORNIA

Giving Voice

The Class of 1980, my class, celebrated its thirty-fifth reunion in May. That may not sound like an exciting topic to share with fellow alumni who read *Harvard Medicine*. But our reunion proved to be such an emotional, intellectual, and logistical success that I thought I'd share some of the hows and whys of its success. Most of all, I want to describe what was completely exhilarating about this event: how we all continue to learn from each other. Through stories, we shared how we had grown and what we hoped we were passing along to others in our profession. In short, going to HMS was just the beginning and not the last, best thing we had done!

As a member of the reunion committee, and editor of our class's reunion report, I had the chance to read everyone's entry. It was a humbling experience—so many powerful stories. If the essays were so illuminating in print, I thought, imagine how stimulating they would be spoken. When talking with my fellow committee members, I realized I was not the only one who thought this. And so, the seed for a nontraditional reunion format was planted.

Instead of organizing long lectures or panel discussions that involved only a hand-

ful of class members, the committee elected to follow a "TED Talk" format. Participating classmates would speak for five minutes on one topic about which each was passionate. Emails, calls, texts, and letters generated a list of twenty volunteers. As you might imagine, these participants spoke on a range of topics: academic and clinical medicine, societal programs, work in the pharmaceutical and the insurance industries, neural sciences, alternative therapeutic modalities, international issues, research administration, and new platforms for scientific publishing. What an unforgettable buffet of ideas and experiences!

Interest in this program brought fifty members of our class to the lunch at which these talks were to be given. That lunch, with families and friends, took place in Building A, now Gordon Hall, in the Waterhouse Room, the very room in which we first met one another more than thirty-five years ago.

Surrounded by formal portraits of physicians from different eras, the Class of 1980 shared their experiences, renewed old and created new friendships. The new format reminded us of the importance of brevity, while each speaker's focus on one idea, pas-

sionately held, reminded us of the excitement of learning. The talks generated many a discussion that continued after the program—even after the reunion! Our use of various online tools has allowed us to keep the discussions going by sharing thoughts, slides, and documents pertinent to the talks.

Group dynamics can be unpredictable, but the Class of 1980 showed it has a mix of creative, talented, and caring individuals who bring out the best in one another. Our reunion was memorable and fulfilled the dreams of many of us to stay curious, to keep learning, and to keep asking how we can continue to contribute meaningfully to medicine.

I am convinced that our class has the ability and kindness to handle the challenges that the changing landscape of medicine continues to bring. This reunion gave each of us the gift of ideas, a lasting and significant gift that is so necessary if we are to continue to embrace what is new in medicine and in life and to develop and lead as caring physicians and individuals.

I wish other classes such thought-provoking and satisfying reunions.

SHARON ANN CLARK '80
SAN MATEO, CALIFORNIA

Photographic Memory

I read with interest the Spring 2015 issue of *Harvard Medicine* and was especially interested in the mention of S. Burt Wolbach, Class of 1903, in "BackStory" written by Susan Karcz. In Spring 1968, my late husband, Laurence H. Green '72, was given a sepia photograph of Wolbach. It shows Wolbach and his colleague, John L. Todd, crossing the Kandong Bolon in Gambia in 1911. I have always wondered about the figures in the photograph; the anecdote about Wolbach reawakened this memory.

MARGOT GREEN
WESTPORT, MASSACHUSETTS

Harvard Medicine welcomes letters to the editor. Please send letters by mail (Harvard Medicine, 107 Avenue Louis Pasteur, Suite 111, Boston, MA 02115); fax (617-432-0446); or email (harvardmedicine@hms.harvard.edu). Letters may be edited for length or clarity.



AND THE AWARD GOES TO ...

Stephen Elledge shares Lasker for the discovery of DNA repair pathway

STEPHEN ELLEDGE, the Gregor Mendel Professor of Genetics and of Medicine at HMS, and professor of medicine at Brigham and Women's Hospital, is a co-recipient of the 2015 Albert Lasker Basic Medical Research Award. He shares the award with Evelyn Witkin of Rutgers University.

Elledge and Witkin were honored for discoveries that have illuminated the DNA damage response, a cellular pathway that senses when DNA is altered and sets in motion a series of responses to protect the cell. This pathway is critical to a better understanding of many diseases and conditions, such as cancer.

The award, widely considered to be among the most respected in biomedicine, was presented to the two researchers on September 18 in New York City.

"Steve is an amazing scientist, mentor, and colleague," said Jeffrey S. Flier, HMS dean. "His insights into the basic mechanisms of the DNA damage response have profoundly enriched our understanding not only of the fundamental genetics of all cellular life, but also of how we conceptualize many diseases and conditions."

Added Elizabeth Nabel, president of Brigham and Women's Health Care, "Steve is courageous and insatiably inquisitive. As a devoted mentor, he is deeply committed to guiding the careers of young investigators."

Elledge often describes the process by which a cell duplicates itself as akin to the duplication of a small city. It is a vastly complex process that requires many levels of intricate coordination. Each cell contains a detailed blueprint for this entire process: DNA.

Yet not every duplication results in a perfect copy. That is because each time a cell makes a copy of itself, DNA is vulnerable to damage, not only from faulty cellular processes, but also from such things as environmental chemicals. As DNA damage accumulates, it profoundly complicates a cell's ability to make a faithful copy of itself. This can lead to serious illnesses, birth defects, cancer, and other health problems.

While Witkin discovered how bacteria respond to DNA damage, detailing the response to UV radiation, Elledge uncovered a DNA-damage-response pathway that operates in more complex organisms, including humans.

Over the years, Elledge and his colleagues elucidated a signaling network that informs a cell when DNA sustains an injury.

Called the DNA damage response, this network senses the problem and sends a signal to the rest of the cell so it can repair damaged areas. The pathway thus helps keep the genome stable and suppresses adverse events such as tumor development.

When individuals are born with mutations in this pathway, they often have severe developmental defects. If the pathway is interfered with later in life, cancer can result.

—David Cameron

Global Reach

Tech-savvy programs reach clinicians, researchers worldwide

USING A BLENDED-LEARNING MODEL that unites students around the world through online tools, in-person seminars and workshops, and geographically diverse collaborative project teams, the HMS Office of Global Education is building a worldwide campus for the School's community of biomedical researchers and health care leaders.

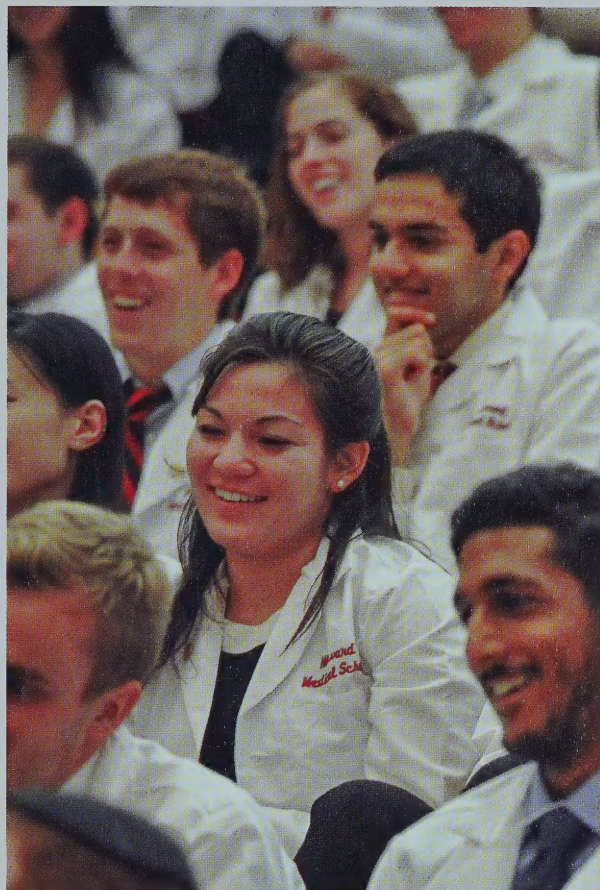
"Our courses take a novel learning approach to delivering the expertise of the School's faculty to current and future global leaders in basic, translational, and clinical research," says Ajay Singh, associate dean for global education and continuing education at HMS. "Those who participate in these courses will, we hope, become part of a truly global network of professionals committed to the mission of Harvard Medical School."

Coursework emphasizes team-based problem solving, which trains individuals of diverse cultural backgrounds and professional experiences to work as a cohesive group toward a shared research or medical outcome. This is a critical skill as health care becomes more globalized and as multinational research teams become the norm, program leaders say.

The blended-learning format strengthens local access to education by allowing admittance into a Harvard-quality program on a competitive basis by those unable to attend a master's-level program outside their home country.

While the first HMS global education blended-learning course, the Global Clinical Scholars Research Training program, is in its third year, the global education team has launched several new programs. One of the new offerings, Introduction to Clinical Research Training, presents students with the fundamental skills for clinical research. Other global education highlights include the Safety, Quality, Informatics and Leadership program, which focuses on patient safety, quality health care delivery, and the role of informatics in clinical settings and the Cancer Biology and Therapeutics program, a joint initiative with the Qatar Biomedical Research Institute. This program is the first from global education to combine basic and applied science in a blended-learning format.

—Jake Miller



A Solidarity of Purpose

The Class of 2019 embarks on a new curriculum

ON AUGUST 4, members of the Class of 2019 at HMS and Harvard School of Dental Medicine received their white coats, symbols of the medical and dental professions.

The day celebrated a medical school tradition while also posing a challenge to the students: You have become part of a community. Savor it and support one another.

In remarks that welcomed students to their calling as healers, Ed Hundert '84, HMS dean for medical education, referenced the Greek god of medicine, Aesculapius. Hundert urged the 165 students gathered in the Armenise Amphitheater to remember the power that touch brings to the healing arts.

The students' backgrounds are varied—eighty-two men and eighty-three women ranging in age from nineteen to thirty-six from thirty-three U.S. states, six other countries and sixty-one undergraduate institutions. Some graduated from college just this year, others a decade or more ago.

The class roster includes fifty-seven students of Asian origin, including Asian Indian, Burmese, Chinese, Korean, Singaporean, Sri Lankan, Taiwanese, Thai, Vietnamese, and Asian other. Another twenty-seven students identified themselves as minorities underrepresented in medicine, a category that includes students who self-identify as Black or African American, Hispanic other, Mexican American, Native American, and Puerto Rican.

This class of students is the first to experience Pathways, a new curriculum that brings students into the clinic nearly a half year earlier than previous classes and also encourages them to become lifelong learners, Jeffrey S. Flier, HMS dean, said.

"You will find yourselves in clinical settings soon, but you will also have more time to think deeply" about which specialty to pursue, Flier said. "With this transformative new curriculum, you have the opportunity to be pioneers as well."

—Elizabeth Cooney and Susan Karcz

BENCHMARKS

DISCOVERY AT HARVARD MEDICAL SCHOOL



FEAST AND FAMINE

Binge-eating cavefish share mutated gene found in some obese people

BLIND CAVEFISH have evolved to be starvation resistant, constantly hungry, and fat but healthy. Interestingly, the genetic mutations that contribute to these characteristics also have been found in the genomes of some obese humans.

Blind cavefish that have adapted to annual cycles of starvation and binge eating have mutations in the gene *MC4R*, the same gene that is mutated in certain obese people with insatiable appetites, according to a study led by HMS geneticists.

The findings, published online July 13 in *PNAS*, reveal more about how vertebrates evolved to have different metabolisms and could provide insights into the relationship between human obesity and disease.

"We know that people have different metabolisms that lead to their gaining weight with different amounts of eating," says the study's senior author, Clifford Tabin, the George Jacob and Jacqueline Hazel Leder Professor of Genetics and chair of the Department of Genetics at HMS.

Blind cavefish in the study live in dark, nutrient-poor caves in northeastern Mexico. In the hundreds of thousands of years since they were separated from their surface-dwelling cousins, they have adapted to their harsh environment by gradually losing their eyes

and their pigmentation and by becoming resistant to starvation. Cavefish achieve the latter by storing massive amounts of fat and by burning it slowly.

The researchers found that after two months without food, the cavefish lost half as much weight as comparable surface populations.

How did the cavefish become so obese in the first place? The scientists found that some cavefish populations evolved to have insatiable appetites; when food does become available, as when it is swept in by annual cycles of high water, the fish eat without limit and store enough fat to sustain them until the next feast. Remarkably, the cavefish live long, healthy lives despite being so overweight.

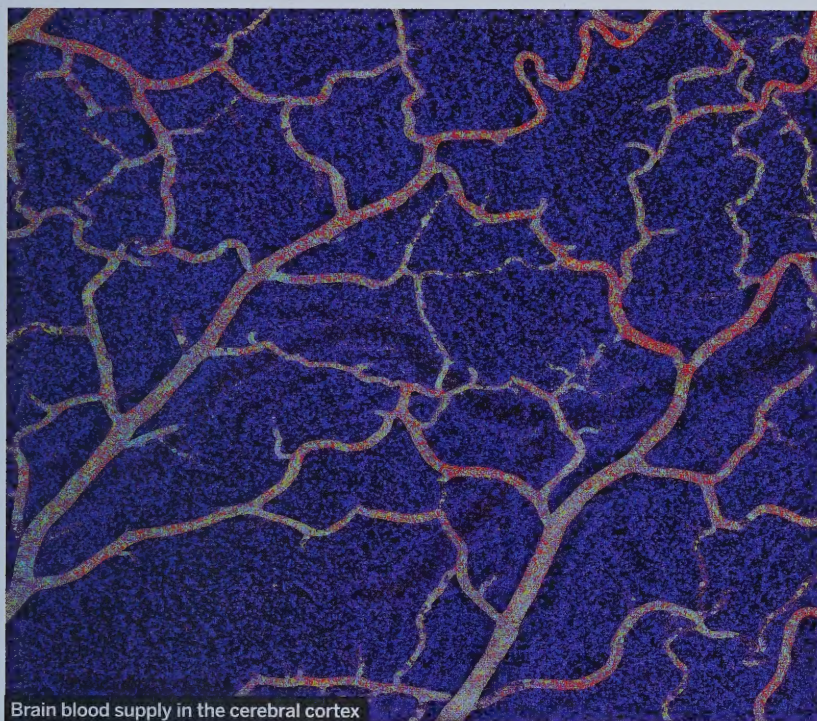
The team analyzed the DNA of fish from several different caves as well as from those in the surrounding surface rivers to determine what genetic mutations could drive the differences in metabolism, body weight, and appetite.

They found that most of the cavefish had mutations in *MC4R*, a gene regulated by leptin, an appetite-suppressing hormone, and by insulin. In humans, *MC4R* mutations—including one that is identical to one in some of the cavefish—are the most common single-gene cause of inherited obesity.

In cavefish, say the team, the mutations appear to reduce the gene's activity by taking the brakes off their appetite suppressor. Although this can be disastrous for humans—children with *MC4R* mutations can't stop eating—the mutations have proven advantageous for the fish.

The researchers are certain other genes are at play in the cavefish and are now looking for additional mutations in the fish, which could in turn inform the search for genes that influence human metabolism and obesity.

—Stephanie Dutchen



Brain blood supply in the cerebral cortex

Crystal Clear

Type 2 diabetes affects memory and learning in older adults

OUR UNDERSTANDING OF THE TOLL that diabetes, particularly type 2 diabetes, can take on brain health has gained definition following research reported by a team of scientists at HMS and Beth Israel Deaconess Medical Center. Their findings show that over a two-year period, older adults with type 2 diabetes developed complications in blood flow regulation in the brain that led to impaired memory and other cognitive problems. The research appeared online July 8 in *Neurology*.

Type 2 diabetes, also known as hyperglycemia, affects more than 44 million people worldwide, including 27 percent of adults over age 65. The condition develops when glucose builds up in the blood instead of entering the body's cells to be used as energy.

The study's findings indicated that on tests of learning and memory the scores of patients with diabetes—which started out eight points lower than scores of patients who did not have diabetes—decreased by an additional 12 percent during the two-year period. Scores of patients who did not have diabetes

remained the same throughout the study. In addition, among participants with diabetes, the brain's ability to increase blood flow when needed for mental processing or other cognitive tasks decreased by 65 percent over the study period. There was no significant change in blood flow regulation among people who did not have diabetes.

The study also showed that higher levels of inflammation were associated with greater decreases in blood flow regulation, even among the participants with diabetes who had good control of their blood sugar.

"In patients with diabetes, excess glucose appears to increase vascular inflammation and impair the endothelial cells that line blood vessels," says Vera Novak, an HMS professor of neurology at Beth Israel Deaconess and the team's leader. "This, in turn, impedes blood flow regulation and disrupts cognitive function."

Adds Novak, "Our findings show that even careful glycemic control did not protect brain function in patients with type 2 diabetes. This study helps explain the mechanisms underlying long-term effects of diabetes on the brain and points to the urgent need for novel treatment strategies to prevent this effect of diabetes on brain function."

—Bonnie Prescott

Pumped

Chronic steroid use increases size of brain's emotion center

AN IMAGING STUDY of the brains of long-term users of anabolic-androgenic steroids has found significant brain structural and functional abnormalities, according to a team of HMS researchers at McLean Hospital. Their findings appear in the July issue of *Drug and Alcohol Dependence*.

Although studies have been published on the cardiovascular, endocrine, and cognitive effects of long-term steroid use, this is the first time researchers have been able to systematically examine changes in the brain from use, says Marc Kaufman, an HMS associate professor of psychiatry, director of the Translational Imaging Laboratory at McLean, and a co-author of the article. The imaging modalities used included MRI, which focuses on brain structure; fMRI, which measures brain activity; and MRS, which looks at levels of different chemicals in the brain.

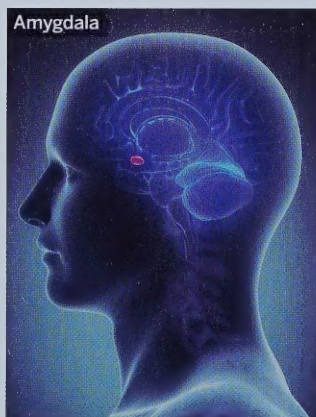
One of the key findings from the structural imaging data, says Kaufman, centered on the amygdala, the region of the brain involved with emotion regulation, aggression, anxiety, and possibly, depression. This structure was more than 20 percent larger in participants who were chronic steroid users than in nonusers.

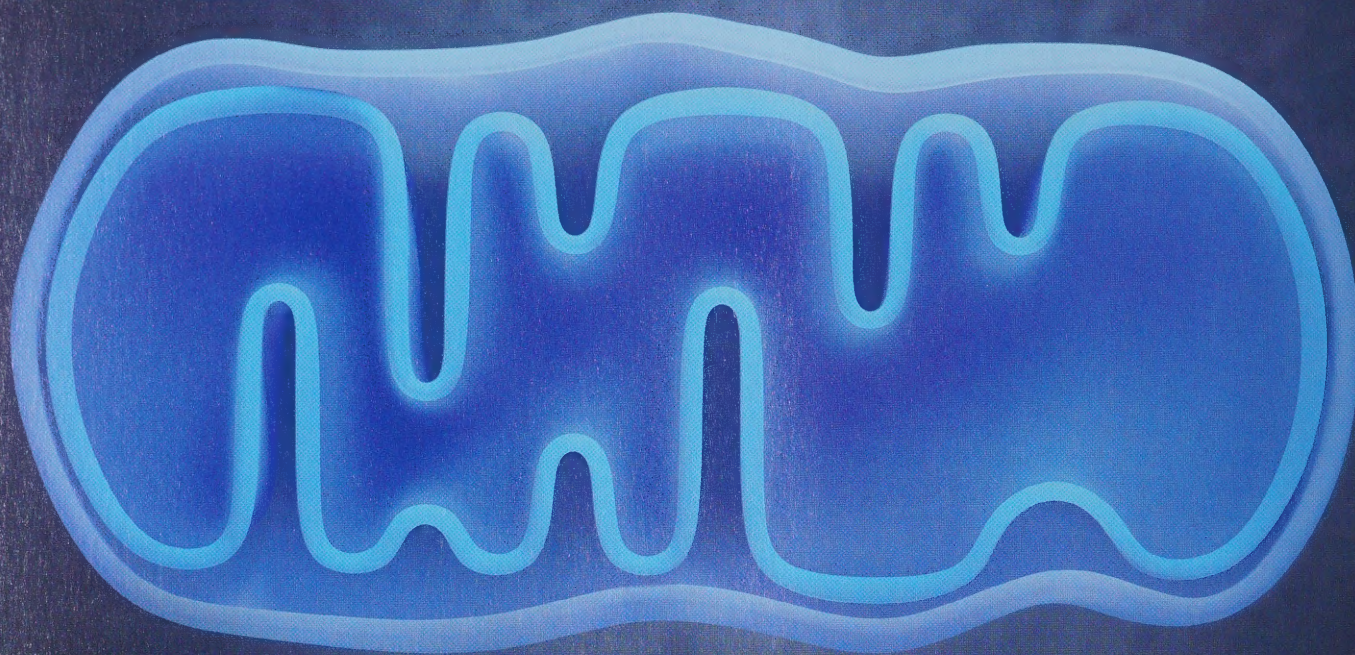
The study uncovered another abnormality among steroid users: a decrease in the brain levels of a sugar known as scyllo-inositol, which is key to preventing neurotoxic proteins from clumping, particularly beta-amyloid proteins, which are known to play a role in the development of Alzheimer's disease and other forms of dementia.

"Anabolic steroids are the newest of the world's major forms of drug abuse," says Harrison Pope '74, an HMS professor of psychiatry, co-director of the Biological Psychiatry Laboratory at McLean, and article co-author. "Widespread use of steroids did not appear until the 1980s in the United States, so

this is a very young form of substance abuse in contrast to other drugs like marijuana and opiates that have been around for thousands of years."

According to Pope, it is estimated that 3 to 4 million U.S. individuals have used steroids at some time in their lives, with approximately one-third continuing to take steroids for long periods of time, often in spite of the adverse effects.





Mitochondrion,
computer-generated image

DAMAGE CONTROL

Researchers connect pathway linked to Parkinson's disease with genes mutated in ALS

WHEN MITOCHONDRIA—the cell's power plants—are sick or damaged, they must be cleared away so the cell can survive. For neurons, this type of quality control is critical; the accumulation of sick or damaged mitochondria in brain cells can contribute to neurodegenerative disease.

HMS researchers now have connected this pathway, the malfunction of which has already been associated with Parkinson's disease and with proteins that are mutated in amyotrophic lateral sclerosis (ALS), the motor-neuron disease also known as Lou Gehrig's disease. Their findings appeared online September 10 in *Molecular Cell*.

Mitochondrial damage triggers activation of two proteins—

PARKIN and PINK1—that tag a mitochondrion's surface with chains of ubiquitin, molecules that signal the cell to get rid of the defective organelles. For more than a decade, faulty PARKIN and PINK1 have been linked with early-onset familial forms of Parkinson's disease, but their role in mitochondrial quality control has only recently been uncovered. In addition, scientists recently have been studying how cells recognize these disposal signals and investigating whether other proteins are involved in the disposal process.

A team of scientists led by Wade Harper, the Bert and Natalie Vallee Professor of Molecular Pathology and chair of the HMS Department of Cell Biology, have described how

PARKIN and PINK1 work with OPTN and TBK1, proteins that help rid cells of deadly bacteria, to clear cells of damaged mitochondria. They found that PARKIN and PINK1 function early in the disposal process by assembling ubiquitin chains that then are tagged to damaged mitochondria. OPTN and TBK1 bind to these ubiquitin chains to target the damaged mitochondria to the autophagy machinery. Both OPTN and TBK1 are mutated in ALS, but how these proteins contribute to this neurodegenerative disease has remained poorly understood.

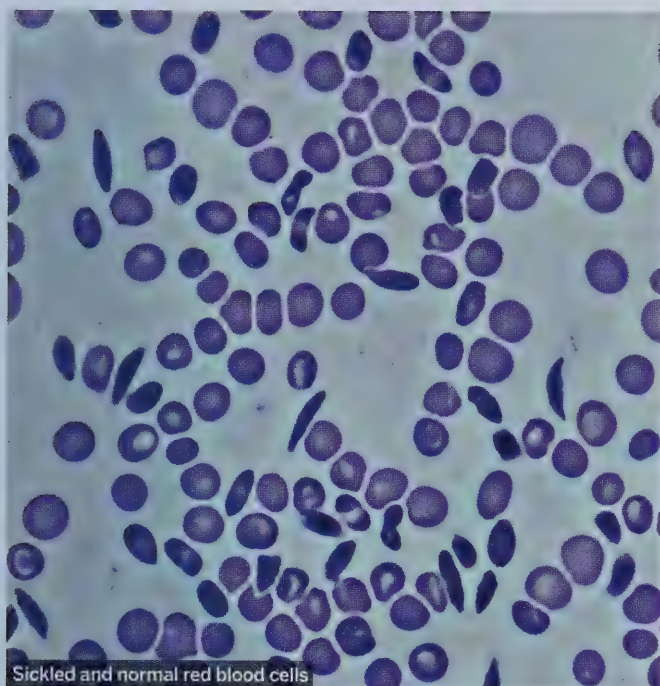
The research team also found that the binding of the OPTN-TBK1 complex to the ubiquitin chains promotes TBK1 activation and further activates OPTN's

ubiquitin-binding activity. This establishes a self-reinforced feed-forward mechanism that is critical for the ultimate delivery of mitochondria to the autophagosome, a part of the cell's system that sequesters and degrades waste material in the cell.

"The surprising thing is that the Parkinson's genes are functioning upstream of a pathway that's mutated downstream in motor-neuron disease," Harper says. "So there is a genetic sensitivity within the pathway that must be different in different cells."

It may turn out, he adds, that this is a general mechanism that cells use to get rid of a variety of damaged material in different kinds of neurons.

—Elizabeth Cooney



Sickled and normal red blood cells

Line Edits

Possible therapeutic target for hemoglobin disorders uncovered

CHANGES TO A SMALL STRETCH OF DNA called an enhancer may circumvent the genetic defect behind sickle-cell disease, say HMS researchers at Dana-Farber/Boston Children's Cancer and Blood Disorders Center.

This finding, reported online in *Nature* on September 16, creates a path for developing gene-editing approaches for treating sickle cell and other hemoglobin disorders, such as thalassemia.

The enhancer identified by the researchers controls the molecular switch *BCL11A*. This switch determines whether a red blood cell produces the adult form of hemoglobin, which is mutated in sickle-cell disease, or a fetal form that counteracts, and is unaffected by, the effects of the sickle mutation. Other studies have found that sickle-cell patients with elevated levels of fetal hemoglobin have a milder form of the disease.

The new study, led by Stuart Orkin '71, the HMS David G. Nathan Professor of Pediatrics at Dana-Farber/Boston Children's; Daniel Bauer, an HMS assistant professor of pediatrics at Boston Children's Hospital; and Feng Zhang of the Broad Institute of Harvard and MIT, was spurred by the discovery that naturally occurring beneficial variations in the DNA sequence in this enhancer decrease *BCL11A* activity only in red blood cells.

Using recently developed CRISPR-based gene-editing tools, the researchers systematically cut out tiny sections of DNA throughout the enhancer in blood stem cells from human donors. They then allowed the cells to mature into red blood cells and found that the amount of fetal hemoglobin the cells produced had increased substantially.

The team's experiments revealed a specific location in the enhancer that, when eliminated, leads to production of high levels of fetal hemoglobin. Additional work showed that these effects occur only in red blood cells.

"We've now targeted the modifier of the modifier of a disease-causing gene," says Orkin. "It's a very different approach to treating disease."

The data provide proof of principle that targeted edits to *BCL11A*'s enhancer in human blood stem cells could be an attractive approach for curing sickle-cell disease and related conditions. —Tom Ulrich

Light Works

Protein-based hydrogel mimics elastic properties of tissues, promotes wound healing

JUST BY ADDING a little light, a new protein-based hydrogel developed by a team of HMS bioengineers can become a substance that mimics many of the properties of elastic tissues such as skin and blood vessels. In addition, the scientists say, finely tuning those properties makes the hydrogel an ideal candidate for use in wound healing. In a paper published online in the July issue of *Advanced Functional Materials*, scientists in the Biomedical Engineering Division at Brigham and Women's Hospital describe the hydrogel's properties as well as the results of its use in preclinical testing.

"So many of the tissues within the human body are elastic," says Nasim Annabi, an HMS lecturer in medicine at Brigham and Women's and a co-senior author of the paper. "If we want to use biomaterials to regenerate those tissues, we need a substance with elasticity and flexibility. Our hydrogel is very flexible, can be made from a biocompatible polypeptide, and can be activated using light."

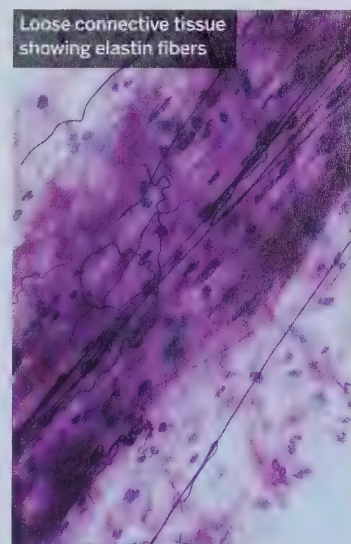
"Hydrogels are widely used in biomedicine," says Ali Khademhosseini, an HMS professor of medicine at Brigham and Women's and a co-senior author, "but currently available materials have limitations. Some synthetic gels degrade into toxic chemicals over time, and some natural gels are not strong enough to withstand the flow of arterial blood through them."

The new material, known as a photocrosslinkable elastin-like

polypeptide-based (ELP) hydrogel, offers several benefits. When exposed to light, strong bonds form between the molecules in the gel, providing it with mechanical stability.

The scientists report that the ELP hydrogel can be digested over time by naturally occurring enzymes and does not appear to have toxic effects when tested with living cells in the lab. The team also found that they could control how much the material swelled as well its strength, finding that the ELP hydrogel could withstand more stretching than that experienced by arterial tissue in the body.

The researchers found that it was possible to combine the gel with silica nanoparticles—microscopic particles previously found to stop bleeding—to develop an even more powerful barrier to promote wound healing.



Loose connective tissue showing elastin fibers



MIND THE GAP

Women are less likely than men to become full professors at U.S. medical schools

FOR NEARLY FOUR DECADES, the number of women attending medical school has increased to the extent that today women represent nearly half of all new physicians. This strong presence, however, is not reflected among the professionals who teach young physicians: Despite efforts to increase equity, the proportion of women at the rank of full professor at U.S. medical schools has not changed since 1980.

According to a study published in the September 15 issue of *JAMA*, women were nearly 13 percent less likely to be full professors than male peers of identical age, experience, and research productivity. The analysis was led by Anupam Jena, an HMS associate professor of health care policy and a physician at Massachusetts General Hospital.

Jena says the persistent gap between male and female promotions is sometimes explained by saying that women are promoted less often because they interrupt their careers during child bearing years, choose specialties that offer fewer opportunities for promotion, or are less productive because, on average, they make work life choices that differ from those of men.

It is also speculated that the pre-existing shortage of senior women faculty members may make it hard for young women trainees to find mentors. These and other factors, the thinking goes, might make women less productive than men, and therefore less likely to be promoted in a system that rewards research productivity.

When Jena and colleagues analyzed data from a commercial social networking service

used by more than a million doctors and more than 90,000 U.S. medical school faculty members, they did find some significant differences in productivity. Women, for example, averaged fewer total publications than men and had fewer papers on which they were the first or last author. They were also less likely to have NIH grants or to have led large clinical trials.

Yet when the researchers compared the genders by age, experience, and research productivity, women were still less likely to be full professors. According to the researchers, this difference was present across all specialties and consistent across medical schools regardless of research funding ranking.

"If the goal is to achieve equity," says Jena, "we need to work on closing that gap."

—Jake Miller

Noteworthy

Analysis of online clinical notes tool shows benefits for patients and doctors

WHAT CAN BE GAINED from allowing patients access to the notes their clinicians write after their visits? Actually, quite a bit, say HMS researchers at Beth Israel Deaconess Medical Center, including improved treatment plan adherence and enhanced error reporting. The research, reported in the August issue of the *Joint Commission Journal on Quality and Patient Safety*, presents an analysis of five years of use of OpenNotes, an online tool that makes health care notes available to patients.

In 2010, Beth Israel Deaconess was one of the pilot sites for the OpenNotes tool. For that study, more than 100 primary care doctors at three hospitals invited nearly 20,000 patients to read their visit notes through a secure website. Patients reported feeling more in control of their health and being better prepared for their visits, while physicians reported little or no impact on their workload. Since 2010, the number of patients who have access to their visit notes has grown to more than five million nationwide.

For the current study, the researchers drew from five years of experience with OpenNotes as well as from data from a new survey and from focus groups to examine key areas of patient safety and quality of care that might be affected by more open communication between doctors and patients.

"Patients and doctors told us that the use of OpenNotes helped them in many ways, including catching medication errors, improved coordination of care for informal caregivers of vulnerable patients, and reduced diagnostic delay," says lead author Sigall Bell '97, an HMS assistant professor of medicine and a member of Beth Israel Deaconess's Division of General Medicine and Primary Care. "In many common safety categories, it appears that having the patient's or an informal caregiver's eyes on clinical notes can help ensure care is safer."

She adds, "Doctors review hundreds or thousands of charts. Patients review one: their own."

According to Bell, patients are interested in participating in their care, noting that "while the responsibility for patient safety still rests primarily with health care organizations, this research shows us what's possible when we make space at the table for patients."

—Kelly Lawman



DINNER CONVERSATIONS

Thinfluence by Walter Willett, Malissa Wood, and Dan Childs
(RODALE, 2014)

reviewed by Elissa Ely

THIS IS A BOOK WRITTEN BY A GIANT (of thought, not size) in the world of nutrition research and a cardiologist who woefully reports that she gained 12 pounds during her internship. In *Thinfluence*, Walter Willett and Malissa Wood have no argument with the fact that obesity has become an unhappy epidemic in this country. But they do argue about its causes: obesogenic factors, they feel certain, are not limited to our own hapless, bereft-of-will selves. "The notion that we are ... islands when it comes to our weight simply isn't true," they write. In a nation that stresses self-determination, we are not fully responsible—at least in this case—for our actions.

Thinfluence is not a scholarly book for medical professionals. Its point is to educate and motivate in simple ways. It starts with a diagram, a visual thesis: four concentric circles featuring examples of internal and external influences that contribute to obesity. Readers should probably keep one finger on that page while reading; as when referring to the cast of characters in a Shakespearean play, they may want to keep flipping back to it.

We are acted upon from within and without, Willett and Wood write. Irresistible internal factors such as genes and emotions are corrosively affected by external factors like physical environment, marketing, and public policy. Pounds result from the combination of one-two punches. The negative synergy that results seems impossible to contend with, yet the authors insist, believably, that it can be.

A large part of the book explains why and how they've found this

to be true. Studies are decoded into straightforward conclusions (one such conclusion—that supportive friendships increase one's consumption of fruits and vegetables—was news to me). There are self-assessments distantly related to take-home quizzes as well as conversational asides (for example, "your emotional eating emergency kit"). Readers taking notes, with the hand that isn't holding a place at the diagram, will find plenty of small and large recommendations, from how to refuse hors-d'oeuvres and alcohol wittily to how to influence food policy.

In some ways, reading this book is like eating healthy fast food: it's palatable, nutritious, and cooked with simple ingredients that are easy to spell. The book is a recipe for dietary and planetary health, and the authors make their points—diet, exercise, community activity, political activism—in a boiled-down, occasionally homespun, but overall endearing, way. "If there were a shopping mall that sold the full range of actions we could take to live a healthier life," they write, "motivation would be the money in our wallets."

On a particularly beautiful autumn day, if a reader is motivated to take an extra-long bike ride instead of finishing one or two of the self-assessment quizzes, Willett and Wood would probably approve. Maybe, in their good health, they are outside themselves, biking in the same direction.

Elissa Ely '87 is a Massachusetts-based psychiatrist.

AUSCULTATION

LISTENING IN ON MEDICAL EDUCATION



Work in Progress

A passion for science, medicine, and people fuels the leadership, and the future, of HMS by Jeffrey S. Flier

I HAD THE OPPORTUNITY TO INTERVIEW MY MOTHER before she died earlier this year at age 95. When I asked her what made her most proud, she answered, without hesitation, “It’s a medical family.” She was referring not only to me, but to my wife, Terry; my daughters, Sarah and Lydia; my brother, Steven; and his daughter, Emily.

My mom was right. We are a medical family. But that wasn’t always the case. In fact, there were no doctors in the family before me. I grew up in the Bronx, New York. My mother was a junior high school mathematics teacher, and my father was a businessman and former World War II pilot.

As a kid growing up in the 1950s and early 1960s, I had two ideas about what I might choose for a career. I had a deep interest in public affairs. When I was elected “mayor” of my elementary school, I absolutely loved it. I enjoyed studying current events and world affairs. A huge admirer of John F. Kennedy, I was devastated when he was assassinated.

My other passion was the world of science and medicine. I admired several of the doctors I met while growing up. I saw the profession of medicine as a way to unite biological science, which I loved, with more humanistic concerns. I was 16 when I entered the City College of New York and, ultimately, decided that a career in medicine would be the most sustaining and rewarding for me.

It’s hard to believe it’s been nearly 45 years since I made that decision. When I reflect on what my mother said, I can’t help but think about what’s made me most proud over the years. And what stands out are the people I’ve worked with. This has especially been true at HMS, where I have had the pleasure of serving as dean for the past eight years.

Last fall, we launched The World Is Waiting: The Campaign for Harvard Medicine. This \$750 million fundraising initiative is all about people. More specifically, it’s about helping people live longer, healthier lives. The campaign is already having a transformative effect on our mission to alleviate human suffering caused by disease through investments in education, discovery, service, and leadership.

In the area of education, our focus is on training the next generation of leaders in science and medicine. We are proud to be one of the only top-tier medical

schools that still adheres to a need-blind admissions policy. This means that an applicant's ability to pay tuition is not factored into our decision about who will be accepted. We also cover the full demonstrated financial need for each accepted student. Last year, 75 percent of students received need-based aid.

Our goal is to raise scholarship funds so that we can uphold our twin values of need-blind admissions and need-based aid. Thanks to generous donors—the majority of whom are HMS alumni and exemplars of our mission in action—we have established sixty-five student aid funds since the prelaunch phase of the campaign began in 2012. We have also raised significant funds to help renovate the Tosteson Medical Education Center so it may better support Pathways, the redesigned curriculum; provide a sophisticated learning environment; and prepare the medical leaders of tomorrow.

In the area of discovery, our aim is to create research collaborations that will help illuminate the cause of disease and advance lifesaving cures. One of our biggest success stories has been the Harvard Program in Therapeutic Science (HiTS). Established in 2013 with philanthropic support, the goal of the program is to rethink the basic and clinical science needed to discover, develop, and deliver better drugs.

In less than two years, HiTS has grown from one employee to eighty-six; opened its flagship Laboratory of Systems Pharmacology; secured \$40 million in federal funding from the National Institutes of Health, the Defense Advanced Research Projects Agency, the U.S. Food and Drug Administration, and the

Gifts earmarked for leadership are critical to continuing our more than 230 years of innovation.

U.S. Department of Energy; and conducted fundamentally new science with faculty, fellows, and students from five partner institutions: MIT, Tufts, and HMS affiliates Brigham and Women's Hospital, Dana-Farber Cancer Institute, and Massachusetts General Hospital.

Gifts from campaign donors have also enabled us to establish ten Quad-based professorships, spanning the fields of education, genetics, global health, health care policy, immunology, neuroscience, and stem cell research. We also established twenty-three affiliate-based professorships, a joint program in translational neuroscience and neuroengineering with École Polytechnique Fédérale de Lausanne in Switzerland, and new centers focused on immunologic diseases with Brigham and Women's, paralysis with Spaulding Rehabilitation Hospital, and, across all affiliates, cancer research with the Ludwig Center.

Our service initiatives focus on building health equity and transforming health systems in the United States and throughout the world by expanding the work of our global health, health care policy, and primary care teams. Gifts from an anonymous donor helped launch our Center for Primary Care in 2012. By partnering with twenty-eight HMS-affiliated adult and pediatric primary care sites in the Boston area, the center is helping to create team-based care models that work to

improve the health of our communities by transforming primary care practice and education. The center now touches the lives of nearly 300,000 patients.

Housed within the Department of Health Care Policy, the new Health Care Markets and Regulation Lab is working to provide policymakers and industry leaders with the scientific evidence and analytical tools necessary to create a fiscally sustainable, high-quality health care system. Our new HMS Center for Global Health Delivery–Dubai is working to increase local and regional health delivery research capacity in the Middle East and the surrounding region. HMS also is co-chairing the Lancet Commission on Global Surgery, which recently published a report that more than doubled previous estimates of the unmet need for surgical care worldwide.

Last, but not least, gifts earmarked for leadership are critical to continuing our more than 230 years of innovation. These gifts provide flexible funds that can be used when and where they are needed most. Some of the initiatives to which I have applied these funds include helping launch HiTS, establishing the Department of Biomedical Informatics, supporting the redesign of our student facilities, and launching our new external education initiatives.

There is no question that this campaign is already having a tangible impact. But our work is not yet done. You don't have to be a doctor or be from a medical family to make an impact on the future of health care. An investment in HMS leverages our biggest strength: human capital. ■

Jeffrey S. Flier is dean of the faculty of medicine at Harvard University.

sotto voce

Neurodegeneration often steals something we consider
quintessentially human—our ability to speak
by Stephanie Dutchen



The man with Parkinson's disease sits quietly in the doctor's office. ■ "We sit in a circle in our living room, and he has nothing to say," his wife reports.

"People don't address him." ■ Daniel Tarsy had deliberately seated the man close to him so they could speak eye to eye. A professor of neurology and a specialist in movement disorders at Beth Israel Deaconess Medical Center, Tarsy knows that Parkinson's can leave people with soft, expressionless voices, difficulty articulating words, and a slowness of thought that makes it hard for them to keep up with the flow of normal conversation. ■ Despite his logistical maneuver, Tarsy finds his attention sliding toward his patient's wife; she's simply more engaged. ■ "Physicians are cautioned against addressing the spouse more than the patient," says Tarsy, "but I'm guilty of it at times. If someone doesn't have much to say and they're older, the assumption is there is not much on their mind, that maybe they're demented. So they get excluded, not just because of their voice

but because of what the other person infers from the voice—that they're just not as bright as they used to be." ■ For those whose lives have been touched

by neurodegenerative disease, the most frightening prospects tend to be the gradual destruction of memory, personality, cognition, or movement. Many people are surprised to discover another troubling outcome: the theft of voice, including the ability to speak or a facility for language. Whether that loss occurs alone or alongside other debilitating symptoms, being unable to talk easily or at all frustrates patients and loved ones and can cost people their hobbies, jobs, relationships, and overall quality of life. ■ Doctors and researchers are striving to understand the basis of these diseases and how they might be stalled or reversed. In the meantime, those who study neurodegenerative conditions that compromise the ability to communicate are remapping language circuits in the brain and investigating why the same disease strikes different areas of the brain in different patients.

Vocal Dynamics

"The halcyon days when I spoke eloquently and with great confidence are gone," wrote Thomas Graboys in his 2008 memoir, *Life in the Balance*. "Nothing, not even speech, is second nature anymore."

A former HMS and Brigham and Women's cardiologist, Graboys developed Parkinson's with Lewy body dementia in the early 2000s. He died in January.

Significant numbers of those who develop neurodegenerative diseases find that their voice or their ability to speak changes in unsettling ways. According to various government institutions and disease foundations, in this country, voice and speech changes affect about 90 percent of the 500,000 to 1 million people with Parkinson's, almost half of the 400,000 to 500,000 people with multiple sclerosis, and about 75 percent of the 30,000 people with amyotrophic lateral sclerosis (ALS). Reliable estimates don't yet exist for the prevalence of rarer neurodegenerative conditions, such as spasmodic dysphonia and primary progressive aphasia, that primarily affect voice, speech, or language, nor for how many of the nation's 5.5 million people with Alzheimer's disease grope for words or struggle to generate or understand complex sentences. On the whole, communication difficulties haven't received as much attention as other deficits associated with Alzheimer's.

Some patients whose voices are affected by certain neurodegenerative diseases may sound strangled or whispery because their vocal cords clench, or loud and quavering because tremor targets the muscles of the larynx. For patients with Parkinson's, the disease not only softens voices but also often robs patients of the ability to detect how quiet they've become.

For others, degenerating motor neurons weaken the muscles involved in speech and make it hard to articulate clearly. Their words may become slurred or their tone monotonous. The uncontrolled movements that give Huntington's chorea its name also can strike people's lips, tongue, and throat, further distorting speech. Some neurodegenerative diseases create "scanning speech," marked by uneven emphasis and irregular pauses between syllables. "It's just a bumpy, uneven kind of speech," says Tarsy. Most people with ALS eventually lose the ability to speak altogether.

Speech impairment can leave patients with the unfortunate choice to stay quiet and risk being considered demented or disengaged,

or to speak and risk being thought drunk or stupid. Producing words becomes physically difficult, and repeating oneself grows tiresome. Speech-language therapy and augmentative devices don't necessarily fix the problem.

The cumulative result is heartbreaking. "At times I get very lonely because people are afraid to talk to me or don't wait for me to write a response," the physicist Stephen Hawking, who has had ALS for more than 50 years, told the BBC earlier this year.

Rhythm and Blues

"I'm well aware of the thought; but I cannot maneuver it to the place in my brain that will allow communication," Graboys wrote. "The neural pathways are disorganized, like some fantastically complex highway system with overpasses and intersections, on-ramps and exit ramps, all leading nowhere. A thought forms, it gets sent down the pike, only to get lost in some cul-de-sac...."

Graboy's suffered from apraxia of speech, a condition that can result when parts of the brain that orchestrate motor control over speech become impaired. Patients know what they want to say, but getting the words out requires intense effort. Perhaps worst of all, they recognize that their vowels and consonants are twisted and that the stress, rhythm, speed, and intonation aren't right—but they can't do anything about it.

"It's painful to produce and painful to listen to," says Kirk Daffner '84, the J. David and Virginia Wimberly Professor of Neurology at Brigham and Women's. "These patients yearn to communicate, but it's such a struggle." Some give up and write or sign instead—unless muscular changes affect their ability to use their hands.

Apraxia of speech is generally considered a planning and production problem, but Bradford Dickerson, an HMS associate professor of neurology at Massachusetts General Hospital, has another theory. He suspects that it's not only a problem of sequencing movements, such as putting syllables

LISTENING IN: Daniel Tarsy (clockwise from right), Kirk Daffner, and M. Marsel Mesulam research the ways in which neurodegenerative diseases affect speech and language.



together to make words, but also a breakdown in timing the parts of the sequence. He got the idea in part because he plays drums.

"If you listen to someone speak, you recognize there's a nuanced, rhythmic process that is generating the accents and punctuation and other parts of normal speech," he says. "I think these patients have a fundamental problem with rhythm in their brain."

Dickerson started asking patients with apraxia of speech to tap simple rhythms with their hands or feet. He discovered they couldn't.

"I think speech is the place where we first notice a problem when people have trouble controlling rhythm or generating rhythm in their mind," he says.

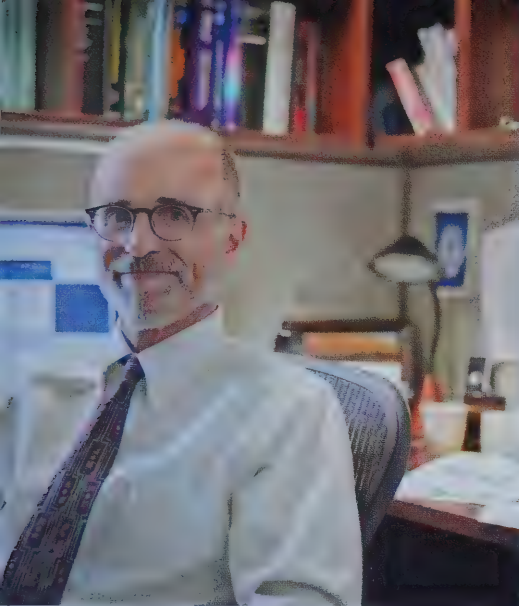
Dickerson notes that models of speech production tend to focus on sequence planning, articulation, and grammar. "One thing I believe neurodegenerative diseases are going to contribute to our understanding of speech," he says, "is the importance of rhythm and timing."

Charting the Terrain

Thirty years ago, neurologist M. Marsel Mesulam '72 asked a patient at what was then Beth Israel Hospital what was bothering her.

"Syntax errors and no articles," she replied. "Words in the my head and cut up."

It sounded as if she'd had a stroke, but imaging showed no evidence of one. Nor did she have memory loss or other signs that would indicate dementia. After seeing a cluster of similarly perplexing patients and immersing himself in the literature of the nineteenth century, where similar cases had



been reported, Mesulam described a neurodegenerative syndrome that hacks away primarily at language. The syndrome is now known as primary progressive aphasia.

Much of today's understanding about how the brain processes language comes from studies of stroke patients, but a large part of the picture remains undefined. Investigating primary progressive aphasia—which can hit areas of the brain that strokes don't usually reach, remains discretely situated within neural regions, and causes damage unlike that from stroke—helps fill in that picture.

Strokes taught scientists that damaging a portion of the back of the brain called Wernicke's area makes it difficult or impossible to understand words and sentences. But Mesulam, who is now director of the Cognitive Neurology and Alzheimer's Disease Center at the Northwestern University Feinberg School of Medicine, found that people with primary progressive aphasia who had damage to Wernicke's area can understand words and have varied success with understanding sentences. He found that patients with sentence-comprehension trouble have neuronal atrophy in parts of Wernicke's area and elsewhere, while patients with single-word comprehension difficulties have atrophy in the anterior temporal lobe, usually on the brain's left side. This region had not been previously linked to language processing.

"We are still in the descriptive phases of cognitive neuroscience," says Mesulam. "The function of the language network is so complicated that every approach you take to try to understand it gives a slightly different perspective. It's like sending a spacecraft to Pluto. You need to piece together pictures taken from different angles and distances to better understand how the world is put together."

Variations on a Theme

Neurodegenerative language loss presents in different ways. Some people lose their grasp on grammar and syntax, while others forget the meaning of words entirely. Some speak haltingly but can understand what others say to them.

The pathology varies as well. In all, about ten neurodegenerative diseases can cause primary progressive aphasia; people may have amyloid beta plaques and tangles characteristic of Alzheimer's disease or defective tau proteins characteristic of frontotemporal dementias. What ties these diseases together is that, for these patients, they erode the language areas first.

Researchers are trying to understand why language regions are more vulnerable in some people than in others. Mesulam has noticed a link to learning disabilities and dyslexia in some families with primary progressive aphasia and is conducting whole-exome sequencing to find out whether those conditions are risk factors.

According to Dickerson, who started a primary progressive aphasia program at Mass General in 2007, the neurodegenerative condition also provides an unusual opportunity to study how language skills devolve over time. Dickerson says that by following the same patient for months or years as she forgets first what "salmon" means, then "fish," then "animals," a physician "can start to predict cognitive functions that are lost or that are dependent on the normal functioning of a certain part of language."

Social Currency

How the gradual decline of verbal communication abilities affects a person can depend on many factors: personality, how intact the rest of the mind is, and whether relationships, jobs, hobbies, and sense of self-worth are language-based.

Losing speech and language means people may no longer be able to engage in rapid repartee, call their loved ones, or read books to their grandchildren. Some people get depressed, engage in self-harm, or take their lives. Others adapt, trying nonverbal pursuits such as painting or gardening.

Only a few drugs have been approved to alleviate neurodegenerative symptoms; there are no cures. As doctors and speech-language therapists try to help patients hold on to what communication skills they have for as long as possible, they also encourage spouses and family members, not immune to depression or frustration themselves, to help by offering suggestions when words don't come, paying attention to nonverbal cues, trying devices that use pictures or written text, and most of all, being patient and understanding.

From writing papers to conferring with colleagues to sharing experiences with loved ones, "we're so dependent on language," says Daffner. "It's amazing, what we're capable of doing with language and speech. When our brains are healthy, it just flows out. It's seamless."

Until it's not. ■

Stephanie Dutchen is a science writer in the HMS Office of Communications and External Relations.





Laryngology is undergoing a high-tech, science-driven interdisciplinary remix
by Elizabeth Dougherty

CORd CHANGES

Roger Egan remembers the precise date he was diagnosed with vocal cord cancer: March 8, 2012. The diagnostic biopsy, taken a few days earlier, had rendered him voiceless, so he had to sit silently as his diagnosis was delivered. But that was not the worst of it. A few days after Egan learned he had cancer, his father died. Again, Egan was mute; he had not yet regained his voice. “When my father needed me most, I couldn’t talk,” says Egan. “I understand the importance of having a voice.” ■ Egan’s voice is fine now, with the deep and resonant tone one might expect from a tall, sturdily built man. He was fortunate; he underwent an innovative type of laser surgery developed at HMS, a surgical option his doctors in North Carolina weren’t aware of. They had offered him radiation, the standard accepted therapy for this type of cancer. It would likely have cured the cancer, but it also would have brought pain and suffering—and the possibility of permanent voice loss.

MATTIAS PASOLI

“I

was twenty-four hours away from going down a completely different path,” says Egan.

As with Egan, patients with voice problems now have more, and better, treatment options. Many of these advances, such as the angiolytic KTP laser used for Egan, have grown from the work of HMS researchers, especially those in the Center for Laryngeal Surgery and Voice Rehabilitation at Massachusetts General Hospital, more commonly known as the MGH Voice Center. Co-directed by Steven Zeitels, the Eugene B. Casey Professor of Laryngeal Surgery at HMS, and Robert Hillman, an HMS professor of surgery, the center has generated new ideas by bringing together the work of experts in disciplines from physics and cell biology to chemical engineering and mobile technologies. Laryngology is thus becoming a sophisticated, science-driven practice that is employing, and exploring, a range of technological options.

Background Vocals

Approximately 7.5 million people in the United States suffer from voice problems, according to the National Institutes of Health. This number will undoubtedly rise as the population ages. “People are living longer and working longer,” says Hillman, “and the aged voice can be weak and hard to understand.”

Overuse can also damage the surface and underlying tissues of the vocal cords, a pair of smooth membranes technically referred to as vocal folds, causing the voice to deteriorate. The types of damage such stress can produce include ruptured blood vessels and the development of hard calluses called nodules or soft growths called polyps. Even very young vocalists can experience damage trying to keep up with demanding vocal training schedules: Some collegiate programs require six hours of singing practice per day.

Surgeries using the green-light emitting angiolytic KTP (potassium, titanyl, phosphate) laser have been performed by Voice Center surgeons to repair overuse injuries in

such famed singers as Adele, Steven Tyler, and Lionel Richie. All have been able to resume their performance schedules. Such results, however, are out of the ordinary. The standard treatments for overuse—blood-vessel cauterization or the surgical removal of growths—can result in scarring or stiffening of the vocal folds. Such changes can limit both the range and strength of a patient’s voice.

Disease also impairs voices. Viral respiratory papillomatosis, for instance, is characterized by the growth of warts on the surface of vocal folds. Smooth tissue becomes lumpy, forming cauliflower-like mounds. In severe cases, the mounds can ultimately block the larynx or trachea. For some patients, the disease recurs so quickly that managing it requires surgery many times a year; for a few, this can mean hundreds of surgeries over a lifetime.

Black Box

The larynx, more commonly referred to as the voice box, is one of the more mysterious parts of the body. It protects the airway to the lungs and houses the vocal folds, forming an obvious but elusive vocal instrument. Peering inside this box requires special equipment, says Hillman. “It’s very dark down there.”

To get a look, in 1807, European doctor Philipp Bozzini devised the first endoscope, called a light conductor, or in his native German, *lichtleiter*. The scope used an external candle to cast light on an internal mirror, thus illuminating the structure of a given cavity—such as the larynx, ear, urethra, or rectum—back to the eye. Throughout most of the nineteenth century, the laryngoscope was essentially a dental mirror. Contemporary laryngoscopes are illuminated speculae that allow a physician to see the vocal folds, which stretch from the front of the larynx to the back and are supported underneath by muscle and a jelly-like substance that keeps them pliable.

Healthy vocal folds vibrate, slamming together to create pulses of air that produce sound waves. In men, the vocal folds vibrate around 110 times per second; in women, 220 times per second, or between two and four times as fast as the beat of a ruby-throated hummingbird’s wings.

In the late 1800s, a primitive laryngostroboscope was developed, allowing laryngologists to visually capture the vocal folds in motion. The stroboscope creates an optical illusion that slows down the motion of the folds, similar to the way that strobe lights



act to slow down the movements of dancers. Although modern computer-driven stroboscopes are still a mainstay of laryngology, HMS laryngologists have begun using high-speed digital video cameras to film the action. These cameras capture up to 10,000 images per second, enough to keep up with the fastest vibrating folds. About a decade ago, these videos revealed the detailed movements that determine whether a voice sounds normal or disordered.

Voices Carry

Perfecting ways to visualize the vocal folds and quantify voice production led Hillman to combine a career as a speech pathologist with voice science, the research side of laryngology. Today, Hillman can barely discuss his work without a visit to his research lab, the place where he evaluates patients’ voices and vocal anatomy before and after surgery or other treatments.

A focal point of Hillman’s lab is a sound-isolation booth filled with sensitive equipment capable of capturing the vibrations of vocal folds. The booth is designed to block building vibrations: twelve-inch-thick walls are deeply insulated while the room itself is suspended from rather than anchored to the building’s structure. In the booth, Hillman and his team use high-speed cameras to identify asymmetries as the vocal folds flap together. They also measure airflow and air pressures generated by the lungs during vocalization and use acoustic measures and other sensors to quantify patients’ vocal function.

Recently, Hillman and his team mobilized his recording technologies by creating an



PRECISION TUNE: Steven Zeitels (left) and Robert Hillman focus their research on developing and refining procedures that rescue damaged or diseased laryngeal structures.

ambulatory monitoring system. Hillman uses the system to track patients as they speak in their daily lives to better understand how voice use and overuse contribute to common voice disorders.

The problem is that no one has yet quantified a healthy limit for voice use. So Hillman's system monitors voice use automatically and tracks a patient continuously for up to a week. The system looks a bit like a police informant's wire—the patient tapes a dime-sized disk to the base of the neck, below the larynx. The disk is wired to a smartphone carried in a pocket or worn on the hip, but instead of recording sounds, the disk picks up vibrations in the larynx before they've been shaped by the mouth.

Hillman has found that voice use, while a factor in some voice disorders, isn't the only factor. For the past three years, his team has been using monitoring technology in an NIH-funded study of heavy voice users, such as teachers and singers, to determine why some, but not all, develop common voice disorders. He is also implementing a biofeedback system that integrates with the new smart watches to alert patients in voice recovery when they enter a voice-use danger zone. "It's the equivalent of the voice therapist following them around," he says.

Hillman's work to objectively measure vocal function has run parallel to the innovations in surgery driven by Zeitels. The work has been crucial for showing that these surgical innovations are, in fact, beneficial to patients. "With objective measures," he says, "you're not depending on the opinion of the surgeon as to how good people sound after being treated for a voice disorder."

Lighting the Way

In 1996, Zeitels met R. Rox Anderson '84, an HMS professor of dermatology and an expert in dermatological laser surgery. Anderson was using a type of angiolytic laser on infants to erase port-wine-stain birthmarks, red marks on the skin caused by abnormal blood vessel growth. Together, the two developed different techniques for use on vocal folds.

Zeitels first used angiolytic lasers to remove precancerous dysplasia and warts associated with respiratory papillomatosis. Initially, Zeitels's team used the new laser on patients under general anesthesia but later realized that the operation, which is quick, precise, and does not cut deeply into healthy tissue, could be performed in the doctor's office on alert patients using topical local anesthesia. For patients with respiratory papillomatosis and precancerous dysplasia, the procedure was a game changer.

In 2003, Zeitels decided to use the KTP laser to treat laryngeal cancer. The light emitted by the KTP laser is preferentially absorbed by hemoglobin in the blood. In vocal fold cancer, the tumor tissue has an abundance of blood vessels, far more than in healthy tissue. When directed at the tumor tissue, the laser heats and vaporizes it while preserving the underlying vocal-fold tissue.

The strategy is similar to the use of anti-angiogenic drugs that target blood vessels. Anti-angiogenics were pioneered by the late Judah Folkman '57, an HMS professor of cell biology. Zeitels had followed Folkman's research, and in 2007, mustered the courage to meet with the man.

For an entrée, Zeitels turned to MIT chemical engineer and biomedical entrepreneur Robert Langer, who had trained with Folkman. Zeitels and Langer were, and continue to be, collaborators on vocal biogel implants that they hope will improve voices damaged by scarring.

Zeitels got his meeting and arrived with a paper he'd written documenting his first ten successful laser surgeries on vocal cord cancer. When Folkman saw the paper, he told Zeitels it needed to be published in the *New England Journal of Medicine*.

The paper had already been promised elsewhere, so Folkman and Zeitels spent three hours discussing the feasibility of using angiolytic lasers to treat other forms of cancer, including laryngeal cancers. As a result of their conversation, Zeitels began injecting the anti-angiogenic drug bevacizumab into the vocal folds of patients with severe forms of respiratory papillomatosis. This treatment approach has been successful, helping all patients with the condition; in many, it has halted the disease.

Tonic Progression

Together, this series of advancements and the voice science that supports them have turned laryngology at HMS into a technologically vibrant and creative field. But those changes have not been widespread in the field. By the time Egan learned of his cancer, the use of the KTP laser for cancer had spread, but not widely. Even today, equipment costs and shortages of trained surgeons have kept the technique from becoming a standard offering outside of major medical centers.

Egan hopes to see more changes disseminated in the field. The human voice is deeply personal, and threats to it can be easy to overlook. Egan in fact ignored his own deteriorating voice for six months. Like many patients, his throat didn't hurt, and his voice deteriorated gradually, with good days and bad. And then, one day, he couldn't even order a coffee.

"The prospect of not having a voice, you can't even think about it," he says. "But once it's happened to you, it's a different conversation." ■

Elizabeth Dougherty is a science writer based in Massachusetts.

When helping a patient prepare for death, talk about life instead

Joanne Wolfe is no stranger to situations charged with the sort of emotional intensity that would shake most of us to the core. Take, for example, the time a group of clinicians under her supervision was caring for a teenage girl who was going to die from a metastatic brain tumor. The team was desperate to discuss with the girl and her mother a potential non-resuscitation order. Without such an order, resuscitation is the default treatment, and the doctors worried that the girl could end up on a ventilator, with her mother forced to decide whether such life support should continue. So, at different times the doctors had presented the girl and her mother with the various options and had asked, "What do you want us to do?" Each time they brought the issue up, however, the girl and her mother evaded the conversation. The doctors came to Wolfe for advice.

by David Cameron



WORDS TO
LIVE BY



"That's often the way it's done," says Wolfe '89, an HMS associate professor of pediatrics and director of pediatric palliative care at Boston Children's Hospital and Dana-Farber Cancer Institute. "Doctors spell out a menu of options without any real context, and the patients are expected to simply choose what they want."

Wolfe recommended a more oblique approach. Rather than asking the patient to make a choice, they asked her to make a list. The girl was encouraged to write down all the things that she wanted, in no particular order, from the sublime to the silly. Nothing was out of bounds.

She put together a document that Wolfe still uses to mentor physicians.

I want a hot tub, the girl wrote. I don't want to be intubated. I want to believe in God. I don't want chest compressions. I want to be able to walk again.

Wolfe continues to be struck by the blended goals the patient put on paper once she was given the opportunity to express herself without conditions. This allowed the girl to find her voice, and from there the decisions flowed naturally.

Eventually she died comfortably, without resuscitation, intubation, or chest compressions.

"The point," says Wolfe, "is to allow the patient's desires to establish a framework, and then you, as a physician, can own the responsibility for making a recommendation."

Doctors are trained to save lives, not to inform patients that they are at the end of theirs. There is, however, a growing consensus in the medical profession that for too long end-of-life conversations have been marginalized to a few brief options that a doctor presents to a patient only after all other interventions have been exhausted. And even then, it occurs rarely. This approach is both a tragedy and source of crisis.

Physicians need to know that there are ways to have these conversations, ways

that can produce effective and profound outcomes. Just as doctors are trained in the latest interventions, they need to learn how to compassionately, effectively, and honestly guide patients through their final days.

Deafening Silence

In the world of medical specialties, palliative care is a newbie. Only in 2006 was it recognized by the American Board of Medical Specialties as an official subspecialty.

Although this may seem inexplicably tardy, consider that as recently as 50 years ago, doctors often withheld a terminal diagnosis from a patient. Susan Block, an HMS professor of psychiatry and medicine and co-director of the HMS Center for Palliative Care, recalls the early days of her own residency, roughly four decades ago, when physicians routinely excluded patients from end-of-life decisions. The doctor called the shots, and there was little transparency.

"This was very typical of the field," she says. "And I was morally troubled by that."

While this sort of paternalism is increasingly the exception, there is still no standardized approach to addressing end-of-life issues. As a result, these conversations happen too infrequently.

"Patients, of course, are ambivalent," says Block, "and doctors are often too attached to the patients or too insecure about their own competencies. It becomes a collusion of silence."

Even when the subject is broached, the conversations tend to happen late. In one study involving patients with metastatic cancer, the first conversation about end-of-life care occurred, on average, 33 days before the patient died, and three-quarters of the conversations were initiated by someone the patient had never before met.

The content of these talks tends to take the form of a data presentation: Here is the reality of your condition. Here are the

options. Here are all the pros and cons of each option. Choose.

"As a palliative physician once said about me, the problem is that we're explain-aholics," says Atul Gawande '94, Samuel O. Thier Professor of Surgery at Brigham and Women's Hospital and author of the 2014 book *Being Mortal*. "We think that what people lack is information. But what they lack is more complicated. People have goals and priorities in their lives besides just living longer—and they want doctors who can understand that and help tune their care to those priorities."

In other words, for physicians to effectively engage patients in end-of-life discussions, they need to fight their tendency to focus on data and instead engage patients on a fundamentally human level.

"This requires transitioning from sounding like medical retailers to being like counselors," adds Gawande, "ones whose approach is, 'Tell me what matters to you, and I'll tell you which options seem best based on that.'"

Voice Activation

There's an irony about end-of-life conversations. When done correctly, they're really not about the end at all. In fact, they are probably more about life than any other conversation you'll ever have. The incongruity is not lost on many palliative-care experts.

"I don't find that phrase helpful with most patients," says Lachlan Forrow '83, an HMS associate professor of medicine and director of palliative-care programs at Beth Israel Deaconess Medical Center. "Kierkegaard said, 'Life can only be understood backwards; but it must be lived forwards.' We don't actually know when it is truly the end of life until someone's died. It's the living that's the most important thing."

Wolfe dispenses with "end-of-life" altogether and instead uses "goals of care."



ON BEING HUMAN: Amplifying the voice that patients have in conversations on palliative care is central to the work of Atul Gawande (far left), Joanne Wolfe, Angelo Volandes, Lachlan Forrow, and Susan Block.

And according to Block, the conversations aren't about dying at all. "These conversations are about goals and quality of life—issues that are meaningful to patients."

The approach taken by Wolfe and her colleagues when talking with a child's family illustrates Block's point:

Tell us about your child as a person. What is she like, and how has that changed since she's become ill?

Tell us your understanding of your child's illness.

What is most important to you and your child?

What are your hopes?

What are your worries?

During difficult times, what gives you strength?

"These kinds of questions help you adapt your approach to the language and values of the family," says Wolfe.

Angelo Volandes, an HMS assistant professor of medicine at Massachusetts General Hospital and author of the 2015 book *The Conversation*, begins these conversations gently.

"I ask, 'What's a good day in your life like? Tell me about a happy day.' I get rid of all the medical language. I get rid of any disease language or prognosis. I try to get rid of any framework of Western medical technology and simply have them tell me what a good day looks like to them."

Speak for Yourself

If the medical field has suffered from a lack of training, incentives, and guidelines concerning such conversations, Block and Gawande are working to change that. For five years they have been working with others to develop and test what Block calls a "serious-illness care program." It is both a program for improving physicians' skills in communicating and planning with patients who have serious illnesses and a support system to ensure that patients who would benefit from these conversations have them.

The program begins with a simple step. A doctor looks over her patient list and for each

individual asks herself one question: If this person were to die within a year, would I be surprised? If the answer is no, then it's time to have a conversation.

The physician, together with others in the program, then receives a two-and-a-half hour training program based on a seven-question guide to what Block calls "patient-centered conversations about serious-illness care goals." Patients are also told in advance that the physician caring for them is going to initiate this conversation and are instructed in how to prepare for it.

Once the conversation is complete, the doctor documents it in the patient's electronic medical record, so that any physician in the patient's care continuum can access it.

A clinical trial evaluating the program's effectiveness is ongoing, and preliminary analysis is encouraging, says Block, suggesting that doctors involved in this program have these conversations earlier and more often than other doctors, and that patients are indeed experiencing better quality of life.

Training Tapes

Volandes is also developing an educational curriculum, but he is tackling the problem from a different angle. Rather than training doctors, he's training patients.

Volandes and his colleagues have created nearly 100 videos in ten languages that offer patients advice on how to "explore goals of care" with their physicians. Other videos describe many of the aggressive medical interventions about which patients with life-threatening diseases are often asked to make decisions. The videos provide concrete demonstrations of how these interventions might affect the patients' daily lives.

"This is really a re-envisioning of the patient-doctor relationship," says Volandes.

So far, more than 200 health care systems, hospitals, hospices, and clinics have made these

videos available, including Mass General. A study at the hospital, authored by Volandes and colleagues and published this year in the *Journal of General Internal Medicine*, showed that only 43 percent of seriously ill patients have a goals-of-care conversation with their physicians. When patients viewed the videos that number rose to 81 percent. The study also found that, in general, about 22 percent of seriously ill patients receive some sort of unwanted intervention. But for patients who have been given access to the videos, that percentage was four.

"If we give patients more knowledge," Volandes says, "we can radically change what happens in health care. Now we have data to show that you can actually budge the needle if you empower patients."

The Human Condition

If, ultimately, end-of-life conversations are less about death and more a focus on life itself, then working in this field is not so much about perfecting medical interventions as it is about perfecting being human—an insight so simple it's radical.

This awareness was driven home to Block a few years back when she went to a parent-teacher night at her son's high school. That day had been particularly brutal for her, heartbreaking and poignant, and she was barely keeping it together. At some point, a father of another student approached her and asked, "How was your day?" She burst into tears. The man, no doubt, was a bit shocked, but Block didn't hold back and told him everything that had happened. When she finished, the man, who worked in finance, looked at her and said, "I would give anything to have a day as close to what it means to be a human being as you've just had." ■

David Cameron is the director of science communications in the HMS Office of Communications and External Relations.





The Sound of One's Own Voice

Voice and speech therapy can help transform identity and aid in gender affirmation
by Stephanie Dutchen

She had tried to feminize her voice on her own, but by the time she came to Barbara Worth for help, her voice was stuck at an unnaturally high pitch. ■ “I think there was a lot of fear in her,” says Worth, a speech-language pathologist at Beth Israel Deaconess Medical Center. “She didn’t want to be outed as transgender.” ■ After decades of presenting as a man, Worth’s patient had overcompensated. Following do-it-yourself programs had caused the muscles of her larynx to tighten to such an extent that she couldn’t produce the lower tones of a typical female speech range, let alone a male range. ■ Worth designed a voice therapy program to undo some of the damage, but progress was slow, and her patient, who didn’t have health insurance, couldn’t afford to continue with therapy. Ultimately, Worth had to discharge her before her goals were met.

◀ Liu Bolin *drawn by*
Hiding in the City –
Sunflowers
2012

LIU BOLIN AND THE KLEIN SUN GALLERY

Sound Track

Voice is a gender signifier. Although some people whose gender identity differs from the sex they were assigned at birth are happy with their voices, others yearn to change the way they sound, often as they transition from one gender presentation to another.

Having a voice that doesn't match one's gender can cause stress and unhappiness, compound anxiety or depression, or trigger gender dysphoria. Some transgender people who aren't comfortable with how they sound won't speak in public or pick up a phone; others won't go out at all.

Developing a natural-sounding voice that matches one's gender expression, whether it is masculine, feminine, gender-neutral, or any of a spectrum of identities, can improve quality of life. Doing so with professional guidance addresses the full range of communication variables and lowers the risk of damaging the delicate tissues of the vocal folds and surrounding structures, damage that can include lesions, hemorrhage, scarring, polyps, nodules, muscle tension, and inflammation.

Although not every case turns out as well as the clinician or patient may hope, voice and speech therapists like Worth are generally able to help transgender patients gain confidence in home, work, school, and social settings.

There are difficulties for those interested in seeking the help of professionals and for physicians who want to help. There's a shortage of speech-language therapists trained in transgender care and a scarcity of hard data about what works. There's also spotty awareness among both doctors and transgender people that speech-language services can help during gender transition. In addition, insurance policies generally don't cover speech-language therapy to assist with gender affirmation.

"I don't think every doctor knows voice therapy is something that can be done to affirm gender identity," says Worth. "Our efforts are successful and can make a difference in these patients' lives."

When Voice Betrays

"I have a wonderful student who presents as a gorgeous woman—makeup, beautiful hair, outfits with heels," says Sandi Hammond, a Boston-area vocal coach and director of the Butterfly Music Transgender Chorus, which she believes is one of only two all-transgender choruses in the country. "She'll walk into a Starbucks, and she's passing, she's passing, she's passing. Then she opens her mouth to order a coffee, and boom."



PITCH PERFECT: Sandi Hammond (clockwise from top left), Ruben Hopwood, and Barbara Worth work with transgender individuals who seek to retrain their voices.

A disconnect between a person's voice and gender expression, even something as unconscious as a sneeze or a laugh, can out them as transgender, potentially costing them their jobs or making them a target of violent acts.

This fear of talking to others "really hampers people's lives," says psychologist Ruben Hopwood, coordinator of the transgender health program at Fenway Health in Boston. "It's not just inconvenient, it's debilitating, and can be dangerous."

A June report from the National Coalition of Anti-Violence Programs found that although reports of overall violence against members of the nation's LGBTQ community declined between 2013 and 2014, homicides rose 11 percent, with hate crimes disproportionately targeting transgender people, particularly women and people of color.

No wonder, then, that many of the nation's estimated 700,000 transgender people strive to masculinize, feminize, or otherwise adjust their voices to better align with their appearance. Given the difficulties of accessing professional care, some will, like Worth's patient, attempt to modify their voices themselves. This carries health risks.



Roughing It

The larynx is exceptionally sensitive to changes in sex hormones, including estrogen, progesterone, and androgens, most notably testosterone. Extended exposure to testosterone permanently lowers the voice, while some studies have found that the larynx is as responsive to estrogen as the cervix, with the female voice undergoing predictable changes at menopause and during menstrual cycles.

Trans men—people who were assigned female at birth but identify as male—who choose to undergo hormone therapy get a head start on voice modification; one of the masculinizing effects of testosterone is that it thickens and lengthens the vocal folds, which tends to lower speaking pitch by about an octave. The voice generally starts deepening within the first few months of treatment and settles into its new pitch in a year or two.

But not all trans men can or want to take testosterone, and among those who do, not all are satisfied with the resulting voice changes. Hopwood has known patients who started smoking to roughen their voices in lieu of taking testosterone.

Estrogen, by contrast, doesn't raise pitch. In addition, trans women—people who were assigned male at birth but who identify as female—can have a harder time overcoming the anatomical and physiological factors that shape their voices, such as trying to keep their voices high and expressive when they're over 6 feet tall and barrel-chested.

"That larynx is big, those vocal folds are big," says Worth. "It can be a challenge, but we can help them modify other aspects of their speech to help them sound more feminine."

The extra hurdles for trans women help explain why speech-language therapists are more likely to hear from trans women than trans men. Coaching videos and smartphone apps are also more likely to focus on voice feminization than on voice masculinization.

Do-it-yourself options can be empowering, allowing transgender people to experiment with their voices in private at little to no cost. A few apps provide quantitative feedback on pitch. Worth, Hammond, and others are optimistic about the potential of certain programs but stress that because of the risks to vocal health, they are best used as a complement to professional voice therapy.

When a patient, particularly a trans woman, is faced with the knowledge that it can take from three months to two years of daily practice to achieve a differently gendered voice, vocal surgery may seem like an attractive solution. A few procedures are available, such as shortening the vocal folds, tightening cartilage, or shrinking or raising the larynx. The results, however, are unpredictable and irreversible, and the best outcomes still require pre- and postoperative voice therapy. Most trans-health specialists recommend against such surgery.

"It's hard when one option for trans women is expensive, high-risk, and fraught

The first thing we tend to hear when characterizing a voice's "gender" is pitch, the human ear's perception of how fast the vocal folds are vibrating.

with peril, while the other requires you to work and work and work and spend money to get frustrated," says Hammond. Still, "habit change is really the best option."

The Gendered Voice

Voice and speech therapy begins by identifying and addressing any underlying pathology and reviewing vocal hygiene. Otherwise, exercising the voice "would be like running on a bad knee," says Hammond. Only when the voice is healthy does attention turn to gender work.

The first thing we tend to hear when characterizing a voice's "gender" is pitch, the human ear's perception of how fast the vocal folds are vibrating. Vocal therapy therefore gives a lot of attention to raising or lowering pitch by training patients to speak within a certain range of tones. Men's vocal folds open and close about 110 times a second, on average. Women's vocal folds average 220 such movements per second, producing a pitch that's about an octave higher than men's. For those who struggle to reach a desired masculine or feminine pitch, a gender-neutral pitch in the middle range can be enough to avoid being misgendered, especially if the patient incorporates other vocal characteristics traditionally associated with their gender. For others, gender-neutral would be the goal.

What are such characteristics? There's intonation, often called the melody of speech. Popular conception is that women use a wider pitch range and engage in rising pitch or "upspeak." There's resonance, the difference between a man's booming chest-based voice and a woman's more contained head-based one. Speech rate and pausing are factors; men supposedly talk faster and more choppy while women stretch out their vowels and use more words. And there's volume (men are louder), clarity (men articulate more), and breathiness (more pronounced in women).

All of these measures and more, of course, are based on stereotypes and exaggerations. They're also culture dependent. Hence, trans patients are encouraged to pay closer attention to how men and women speak by studying the speech of media personalities and that of people in their own communities, so they can spot gender signifiers and choose voice role models. The goal is for the patient to reach for a caricature and break out of lifelong vocal habits, then scale back to something that feels and sounds more natural.

Voice and speech qualities are like a grab bag that trans patients can select from to piece together their desired gender presentation. Small changes can go a long way, especially when accompanied by nonverbal cues that carry gender connotation, such as body language, eye contact, proximity, touching, and smiling, as well as clothes and hairstyle.

Comfort Zone

Trying on a new voice can feel like acting, but, over time, the brain replaces old behavior pathways with new ones.

"When you're learning to play a sport," says Hopwood, "at first you have to think about every muscle movement. With practice, it becomes automatic and you can focus on other things. It's the same with speech."

As more people come out as transgender at younger ages, patients and clinicians wonder whether retraining the voice earlier would be easier than having to undo forty or sixty years of vocal habits. Questions spring up around the possibility: What does suspending puberty mean for the transgender voice? How should older patients be advised on finding their natural pitch after years of affecting unnatural changes to their voices?

As yet, no one has reliable answers to these questions. Whether because it's a young subspecialty or because its subjects have long been stigmatized, Hammond says there is a research "black hole" for transgender voice and speech therapy. A 2012 literature review found that 83 percent of studies on transgender voice and communication sat on the bottom rung of the evidence ladder.

Hammond and others hope that an influx of funding and trained clinicians will close the research gap and help reduce health disparities as transgender communities continue to gain a voice. ■

Stephanie Dutchen is a science writer in the HMS Office of Communications and External Relations.





Song and singing round out the professional and personal lives of physicians
by Ann Marie Menting

HUM A FEW BARS

SUZIE BROWN

"Writing songs brings me joy; it lets me document the phases of my life."

"I know it sounds cliché to say, 'I've always been singing,'" says Suzie Brown '02, "but I have. My parents loved folk music. We would sing Pete Seeger songs while my dad played guitar. When I was older, I would obsessively learn the words to my favorite songs in the Top 40."

Brown still has a life filled with music. A successful singer-songwriter with a number of folk/Americana albums under her belt (her latest was released in late September), Brown tours several times a year with her husband and musical partner, Scot Sax. The music and the tours provide counterpoint to her career as a physician: She works part-time as a cardiologist and assistant professor of medicine at Vanderbilt University Medical Center in Nashville.

This balance was not achieved easily or quickly. Although her years at HMS provided some musical outlets—a role in the Longwood Players' production of *Hair*, open-mic nights singing covers—she didn't think of music as anything but a sideline. Yet toward the end of her fellowship in translational research at the University of Pennsylvania, Brown began doubting her goal of a full-time career in academic medicine.

"All I could think about was music and learning songs. Then I wrote my first song and sang it at an open-mic night. One show led to another, and I realized that playing music made me happier than almost anything else."

"I had finished my cardiology boards," she adds, "so I applied for part-time jobs in cardiology so that I would have more time to dedicate to music."

Music also helps her maintain herself as a physician. "I used to feel a little sapped, dry, as a full-time physician. Having music in my life gives me a way to build myself back up again. I'm just a happier, more giving doctor now."

Brown receives many emails and calls asking her how she achieved success as both a physician and a singer. "It took a lot of hard work and sacrifice," she admits. "There has to be some up-front sacrifice to get where you want to go."

Today, Brown also sings lullabies for her baby girl. Does she hope her daughter will go into music?

"My husband and I hope she'll love music but hope to God she won't be a professional musician," says Brown. "We joke that she'll become an actuary, just to rebel against her musician parents."

LISA SCHAFER

A close-up portrait of an elderly man with a full white beard and mustache, wearing a black tuxedo with a white shirt and a black bow tie. He is looking directly at the camera with a slight smile. The background is dark with out-of-focus yellow lights.

WILLIAM GREEN

"I think perhaps my voice sounds better now than it ever did."

WILLIAM GREEN '54 has retired from his internal medicine practice and now lives in University House, a retirement community in Seattle. Although he participates in the community's monthly sing-along, since 2011 he has also joined his voice with those of about fifty other members of Seattle's Sacred Music Chorale for practices and performances throughout the year. The chorale, which focuses on Christian music, boasts a large roster of female voices. It also, says Green, includes a core of bass voices—his and those of fourteen other men. "We're recruiting," he notes.

It was classmate J. Donald Ostrow '54 who, in 2011, encouraged Green, a recent widower, to join the chorale. Although Ostrow and Green sang together at HMS—"We sang ridiculous parody songs for the Second Year Show"—Green largely was on a vocal hiatus during his years at Harvard College and HMS. Those were years of change for Green, when he moved from his hometown of Berkeley, California, to Boston and transitioned from his family's roots in the Church of Christ to "well, I guess I'd now be labeled an agnostic."

His love of singing, however, always ran deep and true.

"I was part of a family that sang a lot," says Green. "In our church, we sang a cappella. Our director of singing was called the song leader. My grandfather was a song leader, and my uncle was a song leader. I became one during World War II."

"My family occasionally made records," Green adds. "I would sing bass; my grandfather, tenor; my aunt, alto; and my mother

would sing soprano." High school found Green involved in song through glee club and a role in Gilbert and Sullivan's operetta *The Pirates of Penzance*. Then came life as a physician, with little time for song.

His participation in the chorale, however, has revived Green's interest in music, with songs from the chorale's repertoire, and songs from his youth, weaving themselves through his personal life.

Does that mean he sings them in the shower?

Never, he says, then pauses. Well, hardly ever.

“Singing is a lot like medicine—it’s a calling. You feel you have to do it.”

IT MAY HAVE BEEN KISMET or simply a response to efficiency but Christopher Austin’s decision to enter HMS rested on the fact that the School’s acceptance letter arrived before his acceptance to a conservatory did. “I thought, gosh, I got into Harvard Medical School,” Austin ’86 recalls. “I can’t turn that down.”

It was the singing lessons he took during his undergraduate years at Princeton University that stoked Austin’s enthusiasm for singing, particularly for singing opera. “I got hooked,” he says.

“There’s an awful lot of training that’s necessary to be a good singer,” Austin says. “In fact, singing is sometimes referred to as ‘ballet for the vocal tract.’” Gross anatomy class made him appreciate further the importance of vocal training. “It helped me to know what the muscles of the vocal tract looked like. I was aware of their delicacy. What singers require these tiny muscles to do is really Herculean.”

Austin has been making some notable demands on his vocal tract since those college voice lessons. He sang in two operas as an undergraduate. One that was staged during his senior year, *Fidelio*, Beethoven’s only opera, led to an invitation to perform in it at Alice Tully Hall in New York City. So, during his first year at HMS, Austin shuttled between Boston and New York.

While at HMS, Austin sang in three groups: the Boston Cecilia; the choir at Trinity Church; and, as Austin dubs it, “an infamous harmony group called The Testostertones,” a vocal group comprising Austin and three HMS ’86 classmates. Later, a move to Philadelphia led to more opera performances and to appearances with the New York Metropolitan Opera.

“I’ve been fortunate,” says Austin. “I’ve been able to do medicine and sing at the

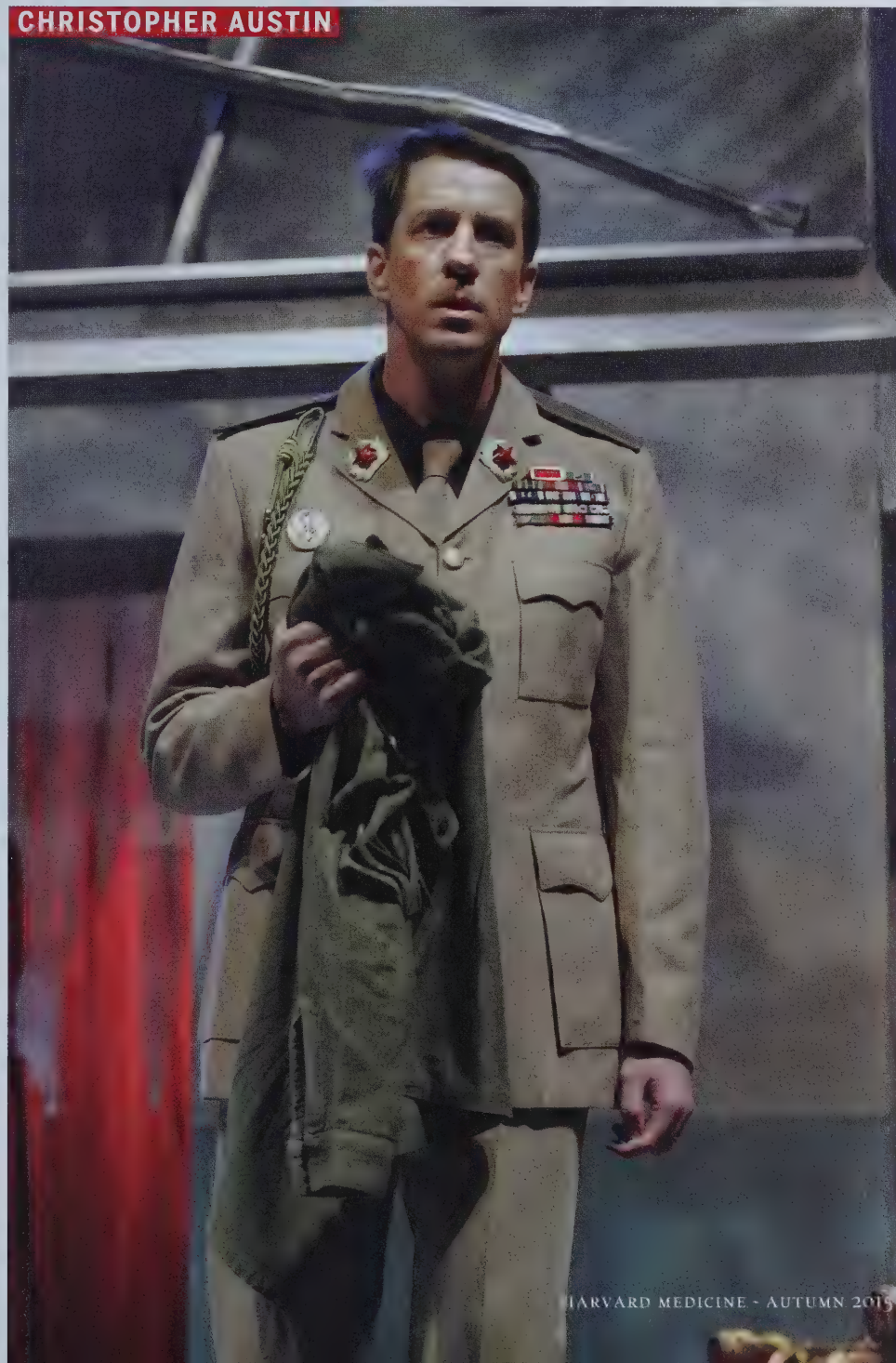
highest levels. I think what drove me to both medicine and music is that they are fundamentally about the same curiosity—the search for what makes humans tick. The kind of crucible that life represents. And both can be healing.”

As director of the National Center for Advancing Translational Sciences at the

National Institutes of Health, Austin has had to put performing largely on hold for the past three years. It’s been tough. During one bereft-of-song period, Austin came home in a bad mood. He recalls his daughter’s treatment recommendation, “Dad, what you need is a rehearsal.”

Austin adds, “She was right.”

CHRISTOPHER AUSTIN



HANDEL, WITH CARE: A deep love of opera and a commitment to pursue a life both as a physician and a singer has allowed Christopher Austin to secure roles with leading companies, such as his appearance as Leone in Handel’s *Tamerlano*, staged by Baltimore’s Opera Vivente.



CHINYERE OBIMBA

AFTER HER FIRST YEAR IN MEDICAL SCHOOL, Chinyere Obimba '12 began a project in Brazil. She was in the home of her host family one day, singing softly to herself. The mother of the family overheard her, and, as Obimba recalls, said, "Wow, when you sing in Portuguese you have no accent at all!"

"That was wonderful," says Obimba, who is a family physician in a federally qualified health center in Seattle. "For me, Brazilian Portuguese is one of the more beautiful languages

"I love the way you can use your voice as an instrument."

for song." In addition to jazz, Obimba ranks Brazil-

ian music, especially bossa nova and música popular brasileira, as her favorite musical genre to sing.

When Obimba speaks of her love of song and singing it's easy to imagine her glowing, transported by the pure joy of song. A member of an extended family of skilled musicians, she sang, and wrote stories, from an early age. "When I was four years old, I would ask my mother to write down the stories I told her." That combined affection means Obimba often learns the stories behind the songs she loves, such as the story behind "Águas de Março" or the "Waters of March," a bossa nova piece written by Antônio Carlos Jobim.

"Jobim was reflecting on what a flood had done to his property," she explains. "He just describes the mundane things around him: a stick, a stone, the end of the road. He's painting a picture. It seems nonsensical, but it's so light and happy that I enjoy singing it."

The power of song to uplift appeals to Obimba. "I concentrated on integrative medicine during my residency and learned that compassion and love for self were important to achieve before trying to heal others. Singing is one of those things I love about myself. Knowing that helps me treat patients who are themselves struggling."

It's only in the past few years that Obimba has allowed herself to consider developing her skill further. Recent performances at a small club in Seattle has fueled this thought.

"It's awesome," she says, "but whenever I start a gig, I introduce myself by saying, 'Well, guys, get ready to hear a shower singer.' But I'm becoming more confident in my abilities."



CARLIN CHI

"Music and singing are integral to my work and my life. They bring me the peace and balance that help me be the type of physician, parent, and person I want to be."

DURING HER THIRD YEAR AT HARVARD COLLEGE, Carlin Chi '98 joined the Harvard-Radcliffe Chorus.

"I'd always enjoyed singing," she says. "In fact, I started singing to myself—folk songs, campfire songs, and such—as a kid, while walking the dog. But I knew I would enjoy being part of a group, making music more formally, and being able to sing big classical pieces." The community aspect and the laid-back nature of the Cambridge-based chorus worked for her.

Chi now works as a family physician at the Petaluma Health Center in Petaluma, California. Every Tuesday, she rushes off to rehearsal with the San Francisco Choral Society. That group's sense of community, as well as its musical repertoire, also suits her.

Works from what Chi describes as the more romantic era of choral music appeal to her. "I actually joined the Choral Society when they were performing Verdi's *Requiem*," she recalls. "I'd never sung it before, and I really wanted to."

Chi can link personal milestones to the music she and the group were singing at a given time.

"There are many people who enjoy Carl Orff's cantata based on the *Carmina Burana*. I have special memories of that work. I rehearsed it for the first time, and was about to perform it with the chorale, when my son was born. I didn't get to sing it in concert that time, but seven years later, I finally got to sing it."

Chi shares her love of music and singing with her patients. "I find that my patients like knowing that I have other interests," she says. "It's similar to how people want to hear about your kids. It's another point of connection."

It's also a way for her to stay grounded, to relax.

"I remember days when I was a resident when I was so tired I didn't want to go to rehearsal," she says. "But I don't even think about that anymore. I know that once I get about halfway through rehearsal, everything else—the stress, the fatigue—goes away. I relax and focus on the music."

Chi hopes that her children will enjoy music as she does. "My partner is very musical, too," she laughs, "so I think there's a good chance they will."

Just for good measure, she sings to them. ■

Ann Marie Menting is editor of Harvard Medicine magazine.





Whether occurring over the fence or in the clinic, conversation requires perceiving the subtleties of voice and body by Susan Karcz

Words alone don't tell tales. When we speak, we use tone, cadence, and body language to telegraph nuances of meaning to others. While words are essential to conveying the message, it's the nonverbal qualities of communication that convey emotional states, the subtext. In fact, research has shown that most of our emotional communication is done nonverbally through facial expressions, gaze, gesture, posture, and tone of voice. In communication, the supporting cast is just as important as the star.

To appreciate—and complete—what's being said, there must be a listener, preferably one who is attentive and responsive to both the meaning of words and the subtleties of voice and body. It's hard to think of a context where the presence of an active listener is of greater moment than in the doctor's office. What does it mean to listen to the illness, and how do the tonal qualities of a patient's, and a physician's, voice contribute to diagnosis and treatment?

Prismatic Perspectives

Because it's so essential to social functioning, the human voice has been called the most important sound in our environment. From birth, our brains are programmed to

respond to characteristics of the human voice, such as tone, pitch, and loudness. Tone of voice shifts as the brain's limbic system processes emotional states such as anger, fear, happiness, and sadness, as well as mood. Vocal tone can also convey social meaning, for instance, sarcasm or deference.

A recent study in the *Journal of Clinical Rheumatology* involving an ethnically diverse group of patients with rheumatoid arthritis investigated how tone of voice, of both physicians and patients, in clinical encounters affected treatment adherence. The researchers found that although physicians and patients reciprocated one another's affect, a physicians' affect, positive or negative, had no effect on treatment adherence, except in one group,



GOOD POSTURE: Fidencio Saldaña (left) and Elizabeth Gauferg prepare students for effective clinical conversations by teaching the principles of patient-centered medicine.

In a group of Hispanic patients, a physician's negative affect was associated with greater treatment compliance at three months when compared with non-Hispanic white patients. When analyzing this result, the researchers speculated that patients interpreted a negative affect as indicating greater concern for their health, which may have then motivated their adherence to treatment.

Patients' tone of voice carried more weight in compliance measures, as patients with poor treatment adherence exhibited a more distressed affect at baseline and at three months than patients with more positive affect.

This finding of what might be considered affective symbiosis speaks to the idea that the clinical encounter works best when the parties involved find a level of understanding. As Francis Weld Peabody, Class of 1907, wrote in the early twentieth century, "unless there is complete confidence in the sympathetic understanding of the physician as well as in his professional skill, very little can be accomplished." One way to get to a mutually agreeable understanding is to ask questions and actively engage with the content and tone of the responses.

Dawn DeWitt '90 would agree. DeWitt, a professor of general internal medicine in the

MD Undergraduate Program at the University of British Columbia Faculty of Medicine and former associate dean in the faculties of medicine both at the University of British Columbia and the University of Melbourne, teaches her students to be alert to emotional cues from patients and to develop powers of perception and observation. "I tell them, 'When you don't know what's going on, it's time to get curious,'" she says. "Curiosity is key." One thing she works on with students is to not let clues drop. "Patients will mention something in the middle of an answer or story," she adds, "and if you don't follow up on it, you're going to miss clues—and cues."

Silence Is Golden

Increasingly, students are seeing patients earlier in their training, and in primary care settings more than in inpatient settings, which gives them the opportunity to establish longer-term relationships with patients and to get to know them over time.

Helping medical students learn how to listen and what to take notice of is a vocation for Elizabeth Gauferg, an HMS associate professor of medicine and psychiatry at Cambridge Health Alliance and founding team member of the HMS-Cambridge Integrated Clerkship at the Cambridge Health Alliance.



In her clinical communications skills classes Gaufberg keeps her focus on patient-centered practice by following the Four Habits Model of Highly Effective Clinicians, an approach developed two decades ago and now in use around the United States and abroad. The model, a guide to conducting a collaborative and fruitful clinical interview, is based on four components of a clinical encounter: invest in the beginning, elicit the patient's perspective, demonstrate empathy, and invest in the end.

As a way of demonstrating empathy, the model suggests that the physician look for changes in the patient's body language and tone of voice, while reminding the physician to look for opportunities to "use a pause, touch, or facial expression" to let the patient know that he is being heard. Demonstrating empathy, according to the four habits model, helps to build trust, which leads to better treatment adherence and outcomes. There is a role on both sides of the exam table, but the physician, being in a position to serve, bears the greater responsibility of being sensitive and observant.

The idea of using a pause, a silence, in conversation is one of the more difficult skills for students to become comfortable with, says Gaufberg. "In the 'giving bad news' exercise, we encourage students to take their cue from a patient's reaction, to, say, news that he or she has metastatic cancer. Sometimes the reaction is silence. And in our society—not just in medicine—we want to fill up silences. Doctors fill up silences with questions or information instead of just allowing patients to experience whatever they're experiencing and giving them time to process and express it."

In teaching the School's Patient-Doctor II course, Fidencio Saldaña '01, an HMS assistant professor of medicine at Brigham and Women's Hospital, works on getting students to feel comfortable with establishing a relationship with the person sitting in front of them by reading body language, interpreting the patient's tone of voice, and sensing what the person is willing to share. Saldaña describes teaching a case in which the patient comes in with a complaint about headache or abdominal pain, but the underlying problem may not be a physical one. In this exercise, the students are coached to read body language as they attend to the patient's story about why the patient is seeking care. "This is something we want to make sure our students are very attuned to."

Advice received during his own years of training has stuck with Saldaña. "One of my mentors always used to ask, 'Who really is this patient? Where do they work? Who do they live with? What is their life like at this point?' We want our students to keep these things in mind. Everyone comes in with a culture and a story, and it's up to us to get a window into what else is going on with them," he says.

Focal Point

Medicine, of course, is not all emotion and psychology. Physicians go through rigorous training in the science as well as the art of medicine. The evidence-based approach to medicine, which started to gain currency about two decades ago, is now beginning

to blend with the traditional approach of patient-centered medicine. This blending, some say, could yield a productive partnership between the scientific and the social.

According to Gaufberg, the seemingly softer approach of patient-centered medicine can contribute to the harder edge of evidence. "It's more than just being nice," she says. "Patients show better diabetes control, for example, if their doctors are more empathetic."

Research published in *PLOS ONE* in 2014 supports this idea, finding a small but statistically significant beneficial effect of the patient-doctor relationship on several objective or validated subjective health outcomes, such as blood pressure, serum readings, and pain relief. Positive physician behaviors listed in the review include the degree of attention to nonverbal signals, the willingness to listen without interrupting and to sit instead of stand when talking with the patient, and the frequency with which appropriate eye contact is made. An intriguing finding is that communications interventions for physicians that are meant to improve the quality of information exchange, such as asking open-ended questions and checking on patients' understanding of their diagnosis and treatment plan, also produce richer interpersonal interactions.

A patient-centered approach can put marks in the plus column for physicians, too. "If doctors attend to the relational aspect of medicine and learn to connect and communicate with patients," Gaufberg says, "they are less likely to burn out. And burnout is linked to other things, like quality of care."

Even small things can serve to build robust connections. Consider the difference it makes when a doctor turns the computer screen toward a patient, forming what is called "the triangle of trust." This gesture allows patient and doctor to review the medical record together, thus creating a story about the patient's life by inviting the patient to co-create her own narrative.

Summarizing the patient's story, letting her correct it and add to it, affirms that her voice has been heard and her tone and manner understood. With this realization, a bond is formed, an alliance forged. The medical becomes personal through the expression of the patient's—and the physician's—voice in the conversation. ■

Susan Karcz is assistant editor of Harvard Medicine magazine.

"Doctors fill up silences with questions or information instead of just allowing patients to experience whatever they're experiencing and giving them time to process and express it."





MANNER AND GRACE: Anne (Nan) Pappenheimer Forbes enjoyed riding her horse, Sorella, around the family's property. During the family's year in Paris, Nan and the children would gather for picnic lunches (above right).

COURTESY OF THE FORBES FAMILY



A WOMAN'S WORK

Anne Pappenheimer Forbes helped shape the field of endocrinology—while mentoring several HMS alumni
by Amalie Kass and Eleanor Shore

WHEN THEY MOVED INTO THEIR HOME in Milton, Massachusetts, Anne Pappenheimer Forbes and her husband, William, were only a few years into their marriage and fresh from stints at Johns Hopkins: Anne, known nearly universally as Nan, as an intern at Johns Hopkins Hospital, and Will, as a medical student.

"We returned to Boston," wrote Nan to Radcliffe classmates for their twenty-fifth reunion, "to a large wooden family mansion which had not been put in order since the nineteenth century and has not been yet." The Victorian house had been in Will's family for three generations; it would become Nan and Will's home for the remainder of their lives. In it, they would rear five children. Around it, the family would, at various times, raise cows, pigs, chickens, horses, and sheep. Into it, Nan and Will would welcome friends, family, and, over the years, more than a few HMS or international trainees. From it, they would commute to their work: Will to the Harvard Fatigue Lab and later to

what was then the Harvard School of Public Health; Nan, for a brief period, to the former Children's Hospital, then to the endocrinology laboratory of Fuller Albright '24 at Massachusetts General Hospital.

Nan would stay at Mass General for four decades. There, often the only female member of the endocrine unit, she would conduct clinical research and mentor interns and fellows who were new to endocrinology. Many of those young men, including Daniel Federman '53 and Mitchell Rabkin '55, eventually achieved their own distinctions in medicine. But Nan, too, achieved recognition. She was only the third woman at Mass General to earn the rank of clinical professor; while at HMS, she was the ninth woman to earn this rank. Her research accomplishments led to her being named one of the first woman members of the American Society of Clinical Investigation and to her papers being included in the Archives for Women in Medicine at the Francis A. Countway Library of Medicine.

Respect for Nan has not diminished. Robert Neer, an HMS associate professor of medicine at Mass General and a research fellow in medicine there in the late 1960s, recently recalled Nan as being “extremely intelligent, fiercely independent, and fearlessly truthful.”

The Prepared Mind

Although Nan’s life was a demanding one, it was one for which she was well prepared. She was born in New York City on November 11, 1911, into an affluent and intellectual family. She received a good education and developed an appreciation of music and the visual arts and a passion for travel. Her father, Alwin Max Pappenheimer, a physician, had interned at Bellevue Hospital before becoming a professor of pathology at Columbia College of Physicians and Surgeons. Nan’s mother, Beatrice Leo, was a talented pianist who made sure Nan and her brothers, Alwin Max Jr. and John Richard, appreciated music.

During World War I, Nan’s father enlisted in the U.S. Army, eventually becoming a lieutenant in the Medical Reserve Corps. In April 1917, he became director of laboratories in his unit, which was preparing to deploy to France. The twenty-one months he was gone were difficult for the tight-knit family. Nan, in fact, feared she would never see her father again.

In 1922, Nan’s parents took the children through Belgium, Germany, Holland, Norway, and Sweden, and to some of the battlefields of France, still furrowed with battle trenches. While in Paris, the children were enrolled in school, the boys in the École alsacienne, a private school for boys, and Nan in a lycée for girls.

Trains and Boats and Automobiles

Upon returning to New York City, Nan attended the Lincoln School, a school founded in 1917 as “a pioneer experimental school for newer educational methods.” During her interview at Radcliffe, Nan said she liked everything at Lincoln, including such extracurricular activities as horseback riding and writing for the school paper. Her plans after college, she said, were medicine or farming.

When, at age 16, Nan entered Radcliffe, it was a liberal arts women’s college referred to as the Annex. Although it was an institution separate from Harvard College, its students were taught by Harvard professors who repeated their lectures on the Radcliffe campus.

As Nan explained to a colleague years later, she was such a rebellious girl that

before her senior year her parents took her on a pedagogical and therapeutic trip around the world starting in 1931. Leaving New York, they spent six weeks in Russia before boarding the Trans-Siberian Railway to Manchuria, then traveled to China and Singapore and to regions then known as Siam and Indochina, before sailing from Hong Kong to San Francisco. They then purchased an automobile and drove across the United States, arriving in New York in February 1932, in time for Nan to start the spring semester.

The trip seems to have served its purpose: Nan was ready to complete her studies. “With two summers at summer school,” she reported to her classmates, “I made up the lost time.” One of the summers was spent studying biochemistry at the Woods Hole marine biology station, a spot familiar to her since childhood. Her father had spent several summers there doing research, and her mother had been instrumental in creating a vacation school for children eager to study science. Nan and her brothers had been students there when they were young.

During summer school, Nan took a biochemistry course; it was her first serious experience with research. In 1933 she graduated cum laude from Radcliffe, simultaneous with completing her first year at Columbia College of Physicians and Surgeons.

Nan and Will married in December 1935, just months before her graduation from medical school.

A Sense of Place

By the time Nan joined Albright’s endocrine unit, first as a volunteer and then as a research fellow, he had already made numerous discoveries and had a group of young doctors assisting him in clinical research. Rounds took place daily at 11 a.m. for every medical attendant and every patient in Ward 4, a ten-bed research unit where patients and healthy participants were intensively studied.

Nan fit well into the group. Intelligent, sensible, and calm, she became Albright’s “physician administrative chief and collaborator,” relieving him of some of the administrative tasks that went with clinical studies. When the United States entered World War II, everything changed. As Nan explained in a Radcliffe reunion report, “the armed services took all his staff, and I became his only (hence invaluable) assistant.”

In 1941 she was second author on a paper on hypopituitarism in *Transactions of the Associa-*



tion of American Physicians and third author on a methods paper in the *Journal of Clinical Endocrinology*, which described a colorimetric assay of 17-ketosteroids in urine. In 1947 in the same journal, she debuted as a first author on the paper “The effect of trauma and disease on the urinary 17-ketosteroid excretion in man.”

Nan conducted studies on a variety of clinical syndromes including one that ultimately carried her name: Forbes-Albright syndrome. Her careful observation of pituitary tumors associated with amenorrhea and galactorrhea convinced her that there must be a human prolactin responsible for the disease, as was later proven.

Albright was so convinced of Nan’s exceptional talent that he nominated her to become a “Young Turk” in the American Society of Clinical Investigators. Albright wrote, “Dr. Forbes has been associated with my research team for seven years. She has contributed a large amount of work and you will find her at the back of many of the better ideas which we have had. She ranks triple A



CONNECTIONS: Nan and William Forbes enjoy the company of three of their grandchildren during the summer of 1976 (clockwise from top); Nan (front row, third from left) stands next to Fuller Albright (fourth from left) in this 1954 photo of members of the Albright endocrine lab; a 1956 portrait of Nan.



on originality.” Nan became a member of the society in the early 1950s, while still a research fellow in medicine at Mass General. In 1977, Nan was promoted to clinical professor of medicine.

During the next several decades, Nan pursued her clinical research and, according to the Countway’s archive, published articles, abstracts, monographs, and editorials on gonadal disorders, pseudohypoparathyroidism, dermatoglyphics, amenorrhea, pituitary tumors, kidney stones, bone diseases, and the connection between menopause and osteoporosis.

On the Road

Nan and Will took the family on extensive overseas trips, including a year in Paris during Will’s appointment as science attaché at the U.S. Embassy. While there, Nan enrolled the

children in the École alsacienne, the same school her brothers had attended twenty years earlier, and embarked on her own research concerning male testicular deficiencies.

To help the children acclimate to their temporary school, Nan joined them for picnic lunches and used the time to counsel them on ways to cope in the sometimes difficult environment. At the end of the school year, Nan and Will took the children on a car trip in Northern Europe. Upon returning to the United States, Nan published her research on testicular function in 1957.

Thirteen years after their time in Paris, Nan spent two years in Shiraz, Iran, where Will had an academic appointment and where she had been appointed assistant professor of medicine at Pahlavi University Medical School. There she taught endocri-

nology to medical students and researched skeletal maturation in Iranian children.

Investing in the Future

According to Nan and Will’s children, their home was a lively place where Nan ferried children to school in the morning and did the cooking in the evening but left dishes in the sink for the household helper to do the next morning. These many years later, the children admit they were happy their mother had a hospital job to absorb some of her prodigious energy. When her mind was not occupied with endocrinologic challenges and children, she raised sheep, rode horses, spun wool, knit, and painted some of the home’s interiors. Various observers and family members acknowledged a degree of domestic chaos but observed nothing of the sort in her academic work at Mass General. She and Will had what the children describe as a warm relationship in which Will supported Nan’s interest in pursuing a demanding but fulfilling career in endocrinology.

In 1978 Nan retired and became an emeritus clinical professor of medicine at HMS. In her report in her Radcliffe class’s sixtieth reunion booklet, Nan wrote, “Retiring after forty years of medical practice I stayed home to care for my husband, who was developing Alzheimer’s disease and to tend to a large garden ... [I also] undertook a job which I highly recommend to other grandmothers; that of providing day care for grandchildren whose mothers work. It is not true that working mothers are not good mothers, but the children are small just when their mothers are hardest pressed ... I gave the children stability and security, while they kept me productively busy, needed, and appreciated.”

In February 1992, Anne Pappenheimer Forbes died of Hodgkin’s lymphoma. Her eldest grandchild, Adam, in his tribute to his grandmother, quoted the last lines of Tennyson’s *Ulysses*:

*Made weak by time and fate, but strong in will
To strive, to seek, to find, and not to yield*

It was, Adam noted, a most fitting epitaph. ■

Amalie Kass is a lecturer on the history of medicine in the HMS Department of Global Health and Social Medicine and the former chair of the Board of the Massachusetts Historical Society. Eleanor Shore ’55 is senior consultant to the HMS Office for Academic and Clinical Programs and the former chair of the Archives for Women in Medicine at the Francis A. Countway Library of Medicine.

Synaptic Sculpting

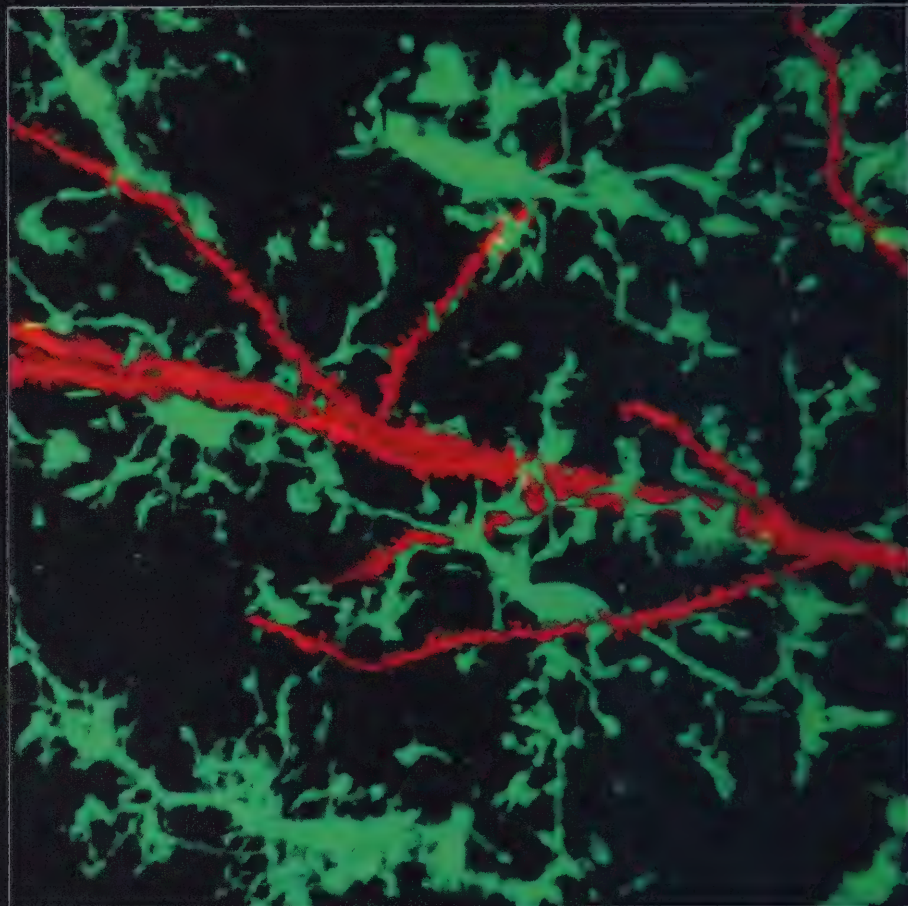
Young brains make connections prodigiously. Thickets of synapses form between neurons early in life, weaving networks of learning and memory.

Before long, however, growing brains need to prune some of their spreading branches. Too many synapses lead to chaos, so at crucial points in brain development, idle synapses are whittled away, clearing the neuronal neighborhood to allow for more precise brain wiring.

This tidying job is undertaken in several ways. One involves the efforts of microglia, specialized immune cells that search and destroy synaptic debris in the brain and throughout the central nervous system. “Glia” comes from the Greek word for glue, and considering their tenacity, the name is apt. Microglia continually survey synapses, leaving the most active ones alone while eliminating the idle ones.

Beth Stevens, an HMS assistant professor of neurology

TIDYING UP: A mouse neuron (red, near right) has microglia (green) dynamically moving around its synapses, whisking away debris; a light micrograph of microglia in the human brain.



in the F.M. Kirby Neurobiology Center at Boston Children's Hospital, has studied microglia in the brain for nearly a decade, ever since, as a postdoc at Stanford, she realized how little attention had been paid to these agents of synaptic sculpting. Her work investigating the molecular mechanisms shared by the immune and nervous systems places her squarely at the intersection of neurology and immunology.

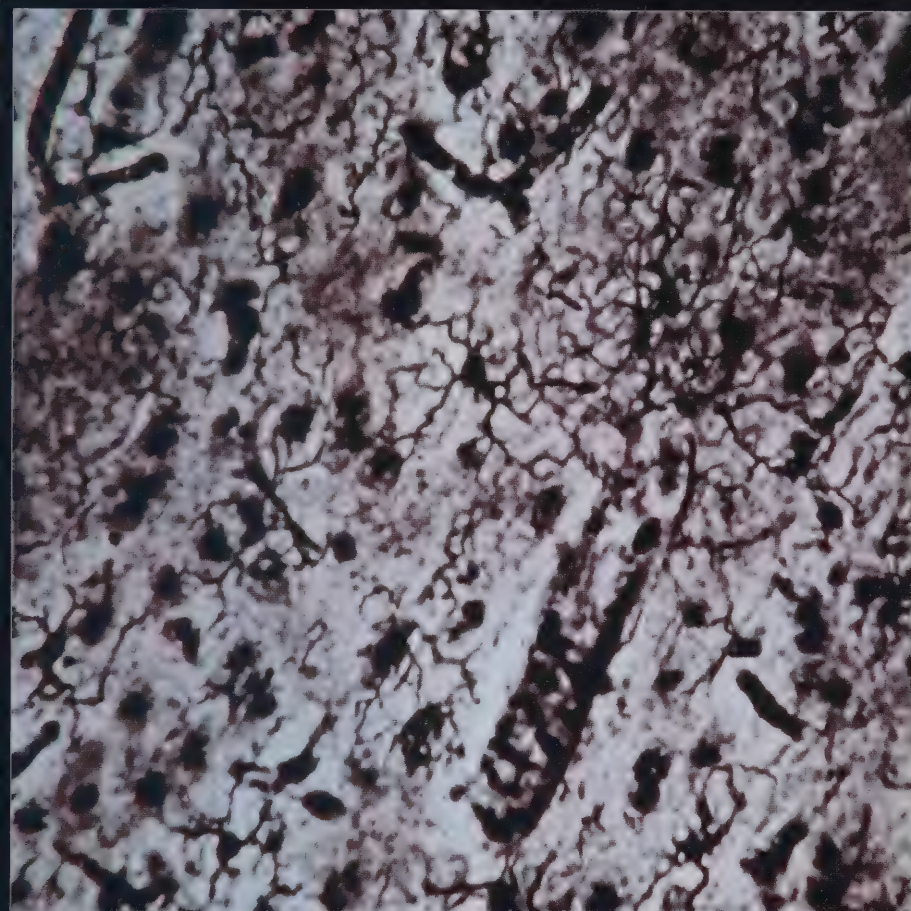
Microglia serve as immune cells in the brain, performing the same functions of surveillance and removal that other immune

players use in the rest of the body to fight invaders. Microglia play defense, too, in at least three ways. First, they rush to sites of injury to mop up intruders and stimulate inflammation in response to damage. Second, they serve as resident phagocytes, cells that remove pathogens and dying cells by engulfing them. And third, they have surface receptors for complement proteins, the immune molecules that tag pathogens and cellular debris with a message that tells microglia to eat the intruders. Stevens and her team discovered that, in the healthy brain, complement proteins tag

extraneous synapses for removal by microglia.

Changes in microglial activity may have a role in disease. In schizophrenia, which, coincidentally, may begin to manifest around the time of normal synaptic pruning during teenage years, brain studies show sparse connections between neurons. In neurodegenerative diseases such as Alzheimer's, synapses almost vanish in areas of the brain devoted to memory.

Stevens hypothesizes that the same pathways that allow synapses to get pruned during



normal development get reactivated to drive synapse loss in neurodegenerative diseases. "These diseases," she says, "are so different in their genetics and in their age of onset, yet they share the features of synapse loss, microglial activity, and the abnormal presence of complement proteins."

"This is like having a good thing go awry," Stevens adds. "A normal developmental mechanism is tipped: Too much of a good thing is not a good thing. But it makes sense to me that your brain might use some of the same mechanisms twice."

Stevens does not suggest that taming microglia could solve neurological diseases by itself. But the cells may represent a target pathway for diagnosis, particularly in Alzheimer's disease, because synaptic loss occurs years before people begin to show signs of deteriorating memory or weakening cognitive function.

For diseases that seem as densely complex as the brain itself, understanding the interplay between microglia, immune cells, and synaptic connections may offer a path through the thickets.

—Elizabeth Cooney



"Beth's work gives us another player and a new signaling pathway to consider in our work on synapse growth and regulation. Glia, and microglia in particular, are so unlike neurons in their structure that we need to set aside our old neuron-centric way of thinking and develop new tools to monitor and manipulate these funny little cells."

—Bernardo Sabatini '95, the Alice and Rodman W. Moorhead III Professor of Neurobiology at HMS

BACKSTORY

FROM THE COLLECTIONS AT HARVARD MEDICAL SCHOOL

WHEN EPHRAIM CUTTER,

Class of 1856, developed “a most earnest desire” to see his own larynx, he got busy and designed a laryngoscope. Cutter thus became part of a tradition of fascination with the human voice and the mechanics behind it.

Manuel García, a Spaniard who was a well-known singing teacher, discovered a way to observe how his own vocal folds moved while singing by using a mirror and illumination by sunlight. He demonstrated this technique on himself at a meeting of the Royal Society of Medicine in 1854; this act, as a news item in a 1905 issue of *JAMA* declared, laid “the foundation of modern laryngology.”

Cutter had heard of García’s demonstration and had seen Prague native Johann Nepomuk Czermak, a physiologist, perform the technique on himself in Paris in 1856 using a more advanced version of García’s laryngoscope.

A physician, a singer, and a physiologist, each with his own reasons to learn more about the larynx and vocal folds, put a personal stamp on the field of laryngology.

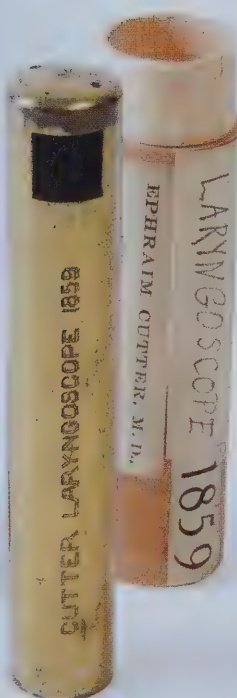
—Susan Karcz



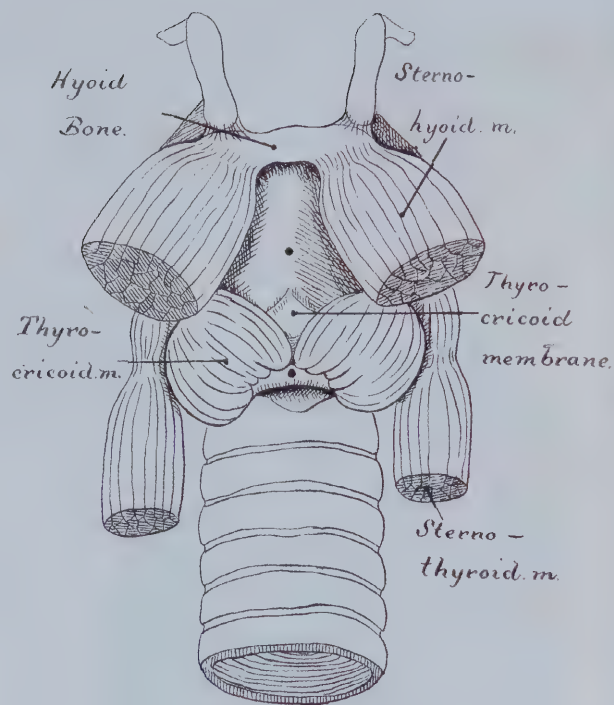
◀ A phrenological head cast of John Thelwall (1764-1834), a professor of the science and practice of elocution in England. Along with the novelist Thomas Hardy, he founded the London Corresponding Society, which campaigned for voting rights and parliamentary reform. He was also the author of a text on the physiological imperfections in speech organs, published in 1814. An entry in a catalog of specimens from the Boston Phrenological Society lists Thelwall's cast in the “Language” category.



◀ This laryngoscope mirror was designed by physiologist Johann Nepomuk Czermak, who is credited with being one of the fathers of laryngoscopy and the first to take a photograph endoscopically. That landmark photo was of his own larynx.



◀ Ephraim Cutter brought his design drawings for this laryngoscope to Alvan Clark & Sons, a renowned maker of telescopic lenses in Cambridge, Massachusetts, where it was manufactured in 1859. He ultimately did not use the tool to view his larynx but did photograph his own larynx using tin mirrors as the reflective medium.



▲ This drawing of the vocal tract is from a nineteenth-century album of color illustrations of vocal folds assembled by Franklin Henry Hooper, Class of 1877, professor of laryngology at Dartmouth College and instructor of laryngology at HMS.

He died of mouth and neck disease in 1892.

▼ Miss Sarah Fuller of Newton, Massachusetts, used cards such as this one to advertise her speech therapy

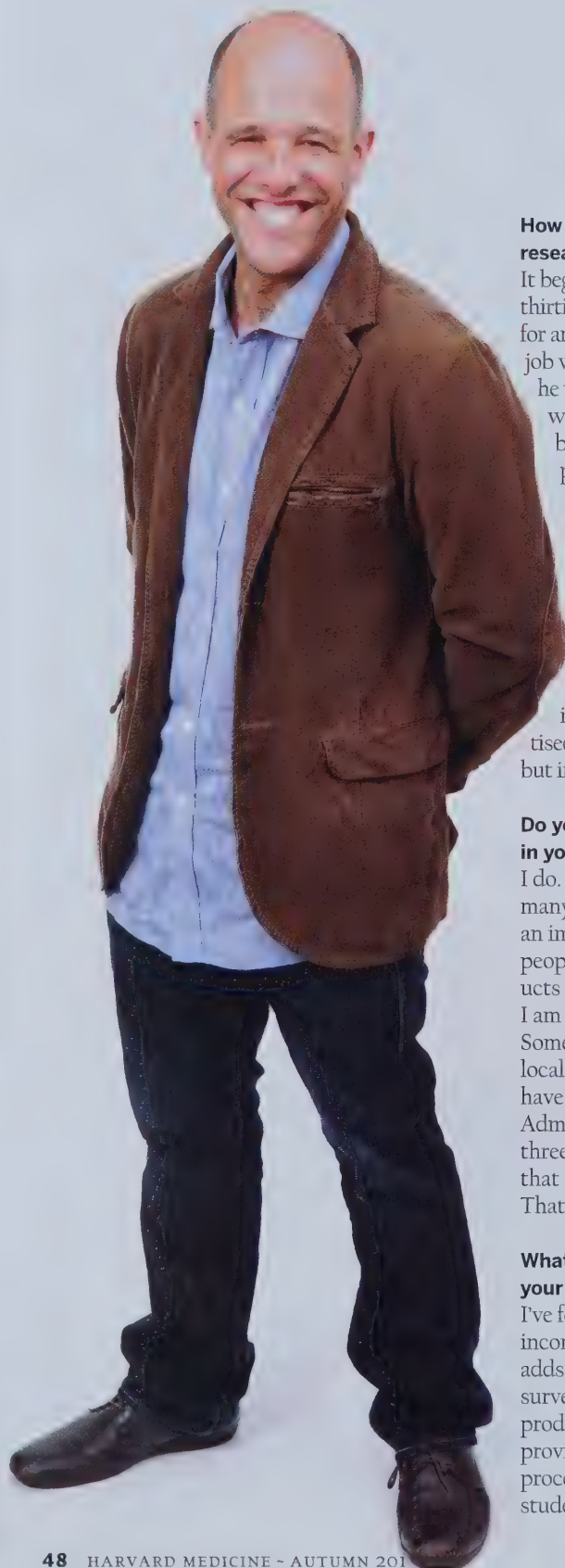
business to correct "stammering, stuttering, and other defects of speech." Fuller trained at the Clarke School for the Deaf in Northampton, Massachusetts, and, for more than four decades, was in charge of the former Boston School for Deaf-Mutes.

*Stammering, Stuttering
and other defects of speech corrected by
Miss Sarah Fuller*

*Arrangements for individual instruction,
or for class lessons, may be made by telephone,
Newton West 308-1
or by mail, addressing 122 Concord Street,
Newton Lower Falls, Massachusetts.*

FIVE QUESTIONS

FOR PIETER COHEN ON DIETARY SUPPLEMENTS



How did you become interested in researching dietary supplements?

It began over a decade ago. A young man in his thirties came to see me after testing positive for amphetamines. That result had cost him his job with the local trash collection service, and he was distraught. He asked whether the weight loss pills he had been taking could be the source of the drug. Although the pills did not list amphetamine as an ingredient, when we tested them we found they contained fenproporex, an amphetamine-type drug that was not approved for use in the United States. I wanted to know how this could happen. Investigating that question eventually led to my researching the safety of weight-loss supplements. I've become especially interested in supplements that are advertised as containing only natural components but in fact contain banned drugs.

Do you take an international perspective in your research?

I do. I care for a lot of immigrant patients; many remind me of my grandfather, who was an immigrant to this country. When I find people marketing bogus weight-loss products to people with limited health literacy, I am compelled to investigate the situation. Some of those investigations have helped local immigrant communities, and some have led to action by the U.S. Food and Drug Administration. That agency recently banned three stimulants that we had studied and that are found in weight-loss supplements. That outcome is very satisfying.

What does clinical practice bring to your research?

I've found it to be profoundly invigorating to incorporate clinical work with research. It adds an important level of engagement. We survey patients for their use of a particular product, recruit them to our studies, and provide them care all at the same time. This process also gets our residents and medical students engaged in research.

Assistant Professor, Cambridge Health Alliance

Assistant Professor of
Medicine, Beth Israel
Deaconess Medical Center

How does teaching factor into your work?

I've remained involved with precept students and residents. As educators, we're teaching students not just about research findings but about how those findings can be incorporated into clinical care. I've developed an interest in the concept of slow medicine, a more conservative approach to caring for patients. In this approach, we teach residents and students the importance of taking careful histories and of performing physicals without depending on unnecessary diagnostic testing or excessive treatments or screening tests.

Is there a common thread to your work in teaching, supplement research, and slow medicine?

The thread is caring for patients. For me, it is a tremendous privilege to have patient care be a part of everything I do. We're always trying to push the needle a little, trying to help our patients be a little healthier. It's about helping as many people as possible by learning from patients, looking at patterns that emerge from clinical work, and then working to boost health in the broader community.

—Angela Alberti



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CONNECT THE DOCS

THE COMMUNITY OF HARVARD MEDICAL SCHOOL ALUMNI

President's Report



When last I wrote, I mentioned that the Alumni Council's principal theme for the foreseeable future is "Con-

nections with HMS." To help make those connections, we asked alumni to host local alumni in their homes on a Sunday afternoon. Thus far, open houses have been held in Ann Arbor, Michigan; Orlando, Florida; Cleveland, Ohio; Santa Fe, New Mexico; and Wilmington, North Carolina. Similar events are scheduled in five different cities this fall. To spark other connections, we asked alumni to reach out to new HMS graduates who are interning in their area. This initiative is being led by Carolyn Olson Walsh '09. I'm pleased to report that several alumni have already volunteered.

Another accomplishment of this year's Alumni Council has been to gain alumni access to several online educational resources. Alumni can now use EBSCO's Academic Search Alumni Edition at hms.harvard.edu/alumni/lifelong-learning/ online-resources. A username and password are required for access. This comprehensive database provides full text as well as indexing and abstracts for thousands of peer-reviewed journals and general periodicals.

Welcome to Michael LaCombe '68, the Council's new president!

Barbara McNeil '66 is the Ridley Watts Professor of Health Care Policy at HMS, founding head of the School's Department of Health Care Policy, and a professor of radiology at Brigham and Women's Hospital.



SISTERS

Alumnus leads team in Haiti in successful separation of conjoined twins

IN MAY, HENRI FORD '84 led an international team of eighteen surgeons, anesthesiologists, and nurses in the successful separation of conjoined twins, the first such operation ever performed in Haiti.

Ford, who was born in Haiti, is the surgeon in chief at Children's Hospital Los Angeles and vice-dean for medical education, professor and vice-chair for clinical affairs, Department of Surgery, Keck School of Medicine, University of Southern California.

When the twins, Marian and Michelle, were born, they were connected at the abdomen. During a seven-hour surgery at the Mirebalais University Hospital, they were successfully separated; twelve days later, they were discharged. According to Ford, the girls are expected to make a full recovery.

The twins, who were part of a set of triplets, were born with their sister, Tamar.

Because the Mirebalais hospital was able to provide the necessary surgical and medical infrastructure and integrate it with the local health system, the surgery could be performed in Haiti, obviating the need to transport the infants to a U.S.-based hospital. Preparation for the procedure included training local clinicians in the specialized postsurgical care the twins would require.

Mirebalais University Hospital, a state-of-the-art teaching hospital on the outskirts of Port-au-Prince, opened in April 2013 to help meet the health care needs of the people of Haiti. In 2010, an earthquake destroyed many of Haiti's hospitals, clinics, and clinical education facilities.

Mirebalais was built through the efforts of a coalition of non-governmental, governmental, corporate, foundation, and academic partners that was led by Partners In Health, a global health care delivery nonprofit cofounded by Jim Yong Kim '88, president of the World Bank Group, and Paul Farmer '88, the Kolokotronis University Professor of Global Health and Social Medicine at Harvard and head of the HMS Department of Global Health and Social Medicine.

—Jake Miller

CONNECT THE DOCS

THE COMMUNITY OF HARVARD MEDICAL SCHOOL ALUMNI



IDENTITY CHECK

Survey of female medical students assesses attitudes on surname changes after marriage

WHAT'S IN A NAME? Quite a bit, if you're a young woman about to begin your career in medicine. At least that's the takeaway from an online survey sent in late 2014 to slightly more than 100 female students at HMS. The survey was the brainchild of Leigh Ann Humphries '17 and grew out of conversations she'd been having with her classmates, most of whom are in their twenties and thirties. The findings appeared online in the January 2015 issue of the *Harvard Medical Student Review*.

"We're starting to make decisions about our careers," says Humphries, "and about how family life and career might intermingle."

Recognizing that decisions to marry often occur during the same span of years in which young doctors

are training, building networks of colleagues, and publishing research, Humphries decided to ask her female classmates about whether they planned to keep or change their surnames after marriage. She developed a short survey, emailed it, then waited for the responses.

She didn't wait long.

"I started sending out the surveys in August 2014," says Humphries. "By October, I had already gathered a large majority of responses." Of the 103 surveys sent, 75 elicited responses.

The respondents included eight women who were married, one who was engaged, and sixty-six who were single. Among those who were single, 65 percent wished to keep their unmarried name; 63

percent of those already married had kept their name. Although Humphries was not too surprised by the results, she was quite surprised by what happened after the surveys were returned.

"The surveys were anonymous," Humphries says, "but a number of women emailed me directly, saying, 'I took the survey and answered in this way. But I want you to have more information on why I answered as I did.'"

The unsolicited explanations indicated the responses were more nuanced and more diverse than she'd expected.

"Certainly many women wanted to keep their maiden names because of their academic accomplishments," says Humphries. "But I was intrigued by the complex reasons respondents gave for their decision to keep their name. Yes, professional identity was a factor, but other reasons included recognizing cultural background, satisfying personal attitudes toward their name, and maintaining individuality and self-expression. One described her interest as a way of expressing 'brand loyalty.'"

Some respondents asked Humphries why she hadn't also surveyed the men in the class. "It would be interesting to ask the men in my class how they would feel about the possibility of their future wives keeping their maiden names," she says. "It would also be interesting to ask them how they would feel about the possibility of taking the names of their future wives, or of hyphenating their names."

Humphries points out that changing one's name is not a small decision for young women who are just beginning to establish themselves in medicine.

"It's on our white coats," she notes. "It's embroidered there."

—Ann Marie Menting



Taking It to the Streets

Physician-author brings the lives of Boston's homeless out of the shadows

FOR THE PAST THREE DECADES, James O'Connell '82 has spent his days, and often his nights, bringing health care to Boston's homeless population. As the founding physician of the Boston Health Care for the Homeless Program, O'Connell practices medicine among those who are often overlooked. He was seeking such a purpose when, at age 30, he arrived at HMS, eager to learn and to find his place in medicine.

"I wanted to figure out how could I make a difference and what would fuel my passion," O'Connell says. "I thought about medicine because I'd always had great admiration for what doctors did. There's something about the practice of medicine that invites you into the lives of people through sharing stories while treating illnesses."

Some of those stories have now been gathered together. *Stories from the Shadows* is a compilation of tales O'Connell has collected over his years with the program, each illuminating

the struggle of living on the edges of society and each shedding light on the difficulty of delivering health care to the city's homeless.

"When I first walked into the program, I thought the nursing staff would be pleased to have a full-time doctor. But they knew I was coming from a world that didn't understand homeless patients," O'Connell says. "One of the nurses instructed me to soak the feet of the patients; I was befuddled. But I quickly came to understand the effectiveness of such simple and humble service. Working at the feet reversed the usual power structure of the doctor-patient relationship and indelibly changed the way I approached the health care of homeless individuals."

Although he often worked more than 100 hours a week, O'Connell ended each day by recalling his interactions with patients and either writing or typing out their stories. He kept the stories in a box.

"I was spellbound," O'Connell says. "I cherished these remarkable characters and didn't want to forget them—or their stories."

"Caring for the homeless," he adds, "quickly unveils the weaknesses in our mainstream systems. We've had to learn how to shape and mold the health care system, including sending our clinicians into the shelters and onto the streets to reach people who are struggling with the immediacy of daily survival. You have to be willing to change and willing to take a risk."

Established in 1985, the Boston Health Care for the Homeless Program now provides acute and subacute, pre- and postoperative, and palliative and end-of-life care in its freestanding 104-bed medical respite facility, the Barbara McInnis House. The program serves more than 12,000 patients annually in more than sixty shelters and outreach sites in Boston.

The book is available at bhchp.org/Stories-fromtheShadows.
—Lauren Massey

CLASS NOTES

NEWS FROM ALUMNI



1956 **60th** REUNION

Paul Altrocchi

I have recently published volumes 6 through 10 of my Shakespeare authorship anthology series, *Building the Case for Edward de Vere as Shakespeare*.

1957

Robert Palmer

I've officially retired but still practice part-time as a consulting physician. I'm happy with my new free time and looking forward to renewed activity. My wife and family are fine.

1958

John Livingstone

My colleague Joanne Gaffney and I have completed a comprehensive textbook for medical students and faculty on psychology and brain science, with special focus on physicians' emotional self-care. The book, *Relationship Power in Health Care: Science of behavior change, decision making, and clinician self-care* is scheduled for publication by CRC Press/Taylor & Francis in December.

1960

Mark Perloth

Retirement is a mixed blessing. My youngest child was married in June, I have retained my medical license and do some consultation, and we are all in grand health.

1962

Morton Goldberg

I recently learned that a rare, inherited muscle disease—known as ryanodine-related myopathy—runs in my family. My family and I have established a new foundation, the RYR-1 Foundation, to support

patient-related research into this currently untreatable disorder. I encourage alumni to learn more about this disease by visiting our website: ryr1.org.

Steven Jonas

I retired as professor of preventive medicine at Stony Brook Medicine in New York in January 2013. As busy as ever, I write a weekly political column for the Greenville Post and other web magazines. My most recent book, published in 2013, is the revised edition of *The 15% Solution: How the Republican religious right took control of the U.S., 1981-2022*.

1965

Leonard Kapelovitz

Abbey and I celebrated 50 wonderful years of marriage with a gathering of all our children and grandchildren.

1967

John Wesley

I, my wife, Connie, and the rest of our family have been blessed with continued good health. We have six thriving grandchildren. This year, I've dedicated my contribution to the scholarship fund to our late classmate, and my former roommate, Paul Schnitker.

1969

Robert Feibel

I have retired from the practice of ophthalmology and am now director of the Center for History of Medicine at the Washington University School of Medicine in St. Louis, Missouri.

1970

John Anane-Sefah

I am sorry I was unable to join you for our 45th reunion, but I plan to be there for our 50th.

1973

John Eichhorn

Stimulated by the J. Eisenberg Patient Safety and Quality Award for Individual Achievement I received from the National Quality Forum/Joint Commission in 2010, the Royal College of Anaesthetists of the United Kingdom named me the current J. Arthur Rank Lecturer. I delivered a series of presentations in England, "The Origin and Evolution of Patient Safety," leading up to the keynote address at the Royal College's annual meeting in Edinburgh and to the College of Anaesthetists of Ireland's annual congress in Dublin. Wonderful trip!

1974

Talmadge King, Jr.

I've been named dean of the University of California San Francisco School of Medicine. During the past 18 years at UCSF, I have served as vice-chair of the Department of Medicine, as chief of medical services at San Francisco General Hospital and Trauma Center, and as chair of the Department of Medicine.

One important part of my job as dean will be to foster ways for us to work together effectively to make the most of the immense pool of talent here.

1975

Steven Swerdlow

I have been awarded the inaugural Berard-Dorfman Founders Award for a senior hematopathologist from the Society for Hematopathology. I'm still hard at work as director of the Division of Hematopathology at the University of Pittsburgh School of Medicine and have many external commitments such as serving as lead editor for the anticipated 2016 revision of the WHO monograph and classification of tumors of the haematopoietic and lymphoid tissues. I am also a trustee of the American Board of Pathology and a member of the residency review committee for pathology of the Accreditation Council for Graduate Medical Education, which reviews training programs in the United States.

Ulder Tillman

I miss so many of you. I am pleased with my career in public health as a physician and county health officer. I have been divorced for years now, and my 30-year-old son died in 2013. Living a "new normal" life with work, church, and friends.

1982

Aaron Appiah

I am still practicing vitreoretinal surgery in Tallahassee, Florida, with no plans to retire yet.

J. Antonio Lopez

In October 2014, I left clinical practice at the Saint Alphonsus Regional Medical Center in Boise, Idaho. I'm currently the cardiovascular medical director of the U.S. medical organization lipid team at Amgen in Thousand Oaks, California.

1993

Nathan Selden

On the first day of 2016, I will become chair of the Department of Neurological Surgery at Oregon Health and Science University in Portland. I've been a member of the neurological surgery faculty there for 15 years and director of the neurosurgery residency program for 10 years. Karen (Hedges) Selden and our three children are thriving. The children are enrolled in an independent day school in the city, and our son and eldest daughter are both taller than us!

1994

John Maa

In 2013, after publishing a series of articles regarding the adverse impact of smoking on surgical outcomes, I became the chair of the University of California Office of the President Tobacco Related Disease Research Program. As a tobacco control champion, I attended the inaugural summit of the White House Initiative on Asian Americans and Pacific Islanders in 2015 and the inaugural World Innovation Summit in Health (WISH) in



CLASS NOTES

NEWS FROM ALUMNI



Doha, Qatar, in 2013. I returned to Qatar earlier this year for the second WISH meeting, where I was pleased to reconnect with Rushika Fernandopulle.

1995

James MacDonald

I continue to do pediatric sports medicine. I am in touch with Bruce Miller, Felix Nunez, Arun Ramappa '96, and Jon Grayzel. All the best to everyone.

1996 20th REUNION

Jonathan Bailey

I was named the associate medical director of the University of Illinois Urbana-Champaign College of Medicine Department of Surgery. In this position I oversee the divisions of Plastic and Reconstructive Surgery, Ophthalmology, Otolaryngology, Head and Neck Surgery, and Oral and Maxillofacial Surgery. I am a clinical associate professor there and the residency program director in oral and maxillofacial surgery at Carle Foundation Hospital in Urbana-Champaign. My wife,

Karanetta, and I have four children, ages three to twenty-two.

1997

Kerry Ressler, Jr.

I am delighted to finally be returning to the Boston area after 18 years at Emory in Atlanta. In August, I began appointments as chief scientific officer and chief of the Depression and Anxiety Disorders Division at McLean Hospital in Belmont, Massachusetts, and as professor of psychiatry at HMS. I also hold the James and Patricia Poitras Endowed Chair in Psychiatry at McLean.

As chief scientific officer I oversee the hospital's comprehensive research enterprise, enhancing the breadth and depth of the scientific portfolio, promoting research collaborations, and advancing a vision for improved lab facilities. As McLean's inaugural chief of the Depression and Anxiety Disorders Division, I will work to improve communication across clinical operations, while working with researchers with an interest in depression and anxiety. I look forward to working with others in Boston and across Harvard programs.

Finally, on a family note, my wife, Betsy, and I are doing great, with our first of three sons off to college this year! Best wishes to my former colleagues and classmates. I hope to catch up soon.

1999

Sangeeta Bhatia

I was honored and grateful to receive the Heinz Award in the Technology, the Economy and Employment category for my work in growing artificial human "microlivers," which can be used in screening for drug toxicity. This award also recognized my advocacy for the advancement of women in engineering and of girls in STEM fields.

Share Your News

If you have updates you'd like to share in Class Notes, you can submit them easily and securely to classnotes@hms.harvard.edu. Be sure to include your full name and class year.

OBITUARIES

REMEMBERING DISTINGUISHED LIVES

1930s

1936

Marlow B. Harrison
May 11, 2015

1939

John B. Stanbury
July 6, 2015

1940s

1945

William H. Simpson
September 12, 2015

1946

Alvin S. Aldrich
August 28, 2015

J. Vincent Arey
June 16, 2015

Charles O. Carothers
August 16, 2015

1947

Frederick W. Malkinson
September 7, 2015

Richard S. Ross
August 11, 2015

Armand D. Versaci
June 17, 2015

1948

Jack B. Davis
July 7, 2015

1949

John W. Keller
September 11, 2015

Alexander Rich
April 27, 2015

1950s

1950

Robert C. Coe
July 17, 2015

M. Patrick O'Meara
June 3, 2015

1951

George K. Summer
July 8, 2015

1952

James G. Andersen
August 27, 2015

Harold L. Atkins
May 1, 2015

1953

Edwin W. Brown, Jr.
May 23, 2015

Mathew I. Gelfand
August 11, 2015

Frederik C. Hansen, Jr.
August 23, 2015

1954

Peter R. Dallman
August 20, 2015

Franz R. Schneider
April 25, 2015

1956

Donald L. Schotland
August 13, 2015

1957

Emanuel S. Hellman
May 20, 2015

Arthur S. McFee
June 20, 2015

George S. Weber
May 3, 2015

1958

Allen W. Cheever
August 29, 2015

David D. Christensen
June 18, 2015

Robert S. Rosson
May 8, 2015

1959

Lois Barth Epstein
February 6, 2015

Joan W. Flacke
June 29, 2015

1960s

1960

George J. Shaka
September 7, 2015

1963

Gordon C. Vineyard
May 5, 2015

1965

Arthur E. Reider
August 13, 2015

James W. Wallace
August 20, 2015

1966

Edwin H. Cassem
July 4, 2015

1968

Patricia C. Adams
April 25, 2015

John M. Templeton, Jr.
May 16, 2015

1970s

1970

James H. Shelton
September 13, 2015

1971

J. Andrew Billings
September 6, 2015

1972

Alexander W. Clowes
July 7, 2015

1973

Carolyn G. Dedrick
May 9, 2015

1980s

1986

Linda L. Fletcher
August 13, 2015

Arshavir Michael
April 15, 2015

David C. Seldin
June 27, 2015

This listing of deceased alumni includes those alumni whose notices of death were received between April 25, 2015, and September 25, 2015. Links to full obituaries of these alumni can be found at hms.harvard.edu/memoriam.

If you know of an HMS alumna/us who has died recently, please email the link to the obituary to hmsalum@hms.harvard.edu.

TAKING A HISTORY

PROFILE OF GARY GIBBONS, CLASS OF 1984



CLAIM TO FAME

Director of the National Heart, Lung, and Blood Institute (NHLBI), National Institutes of Health

ASKED AND ANSWERING

Gary Gibbons '84 has always been curious. "One of my early memories is of my parents, who were both schoolteachers, giving me books that literally were called 'How and Why,'" he says.

That curiosity kindled an early interest in science and engineering. "I had my own chemistry set, all that sort of thing," he says. "I was very curious about how things worked."

Science led him to medicine and to HMS, where he met A. Clifford Barger '43, his first-year physiology professor. "I remember distinctly asking him why African Americans had more high blood pressure and cardiovascular complications than other groups," he says. "Even though he was a world expert on blood pressure, he turned the question around and challenged me to ask and answer it myself."

A summer position in Barger's laboratory led to two more, each spent investigating blood pressure regulation. "That work transformed the trajectory of my life and career," says Gibbons.

COLLECTED WISDOM

Family influences fostered Gibbons's commitment to hard work and also strengthened his interest in eliminating health disparities.

"My grandmother has always been my benchmark for hard work," says Gibbons. "She was a sharecropper's daughter in rural Georgia, with access to no more than an elementary education. She worked

into her seventies as a domestic cleaning the floors of others."

His work in addressing health disparities led to faculty positions at both Stanford University and HMS, to Morehouse School of Medicine in Atlanta as the founding director of its Cardiovascular Research Institute, to an appointment as chair of Morehouse's Department of Physiology, and, in 2012, to his position at the National Heart, Lung, and Blood Institute.

Gibbons' family—particularly his three adult children—inspires him. So do the members of his church. "My other family is my church family," he says. "It has been an important contributor to my life and helps sustain me."

PERSONAL BEST

At NHLBI, Gibbons is dedicated to knowledge generation, especially for heart, lung, blood, and sleep disorders.

"I get up every morning and embrace the fact that I have responsibility for the work of thousands of employees who are focused on generating new knowledge that will affect the health of the nation."

Gibbons is also dedicated to developing the next generation of leaders by investing in their training and development. Medicine, he thinks, offers its professionals an unprecedented opportunity to contribute not only to the body of scientific knowledge but also to our collective and individual well-being.

"I can't think of a better life path than the one that I'm on," he says. "If I could turn back the clock, I'd do it again."

—Katie DuBoff



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- Cavefish and Human Obesity: a video
- A Different Kind of Love Song: a story of Boston's transgender chorus

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